

ماجستيد تناسليه (7)

Erectile dysfunction

د/هانی ابوالوفا

2017

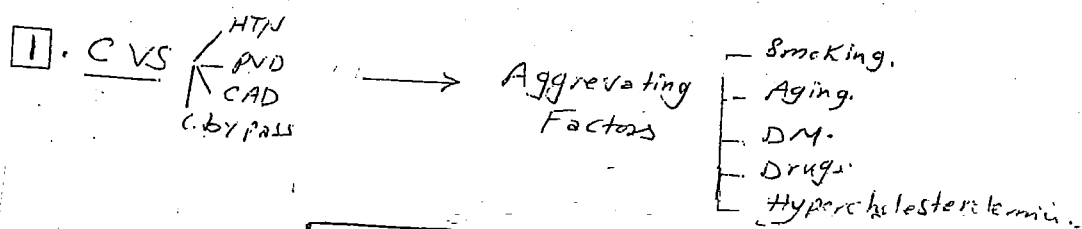
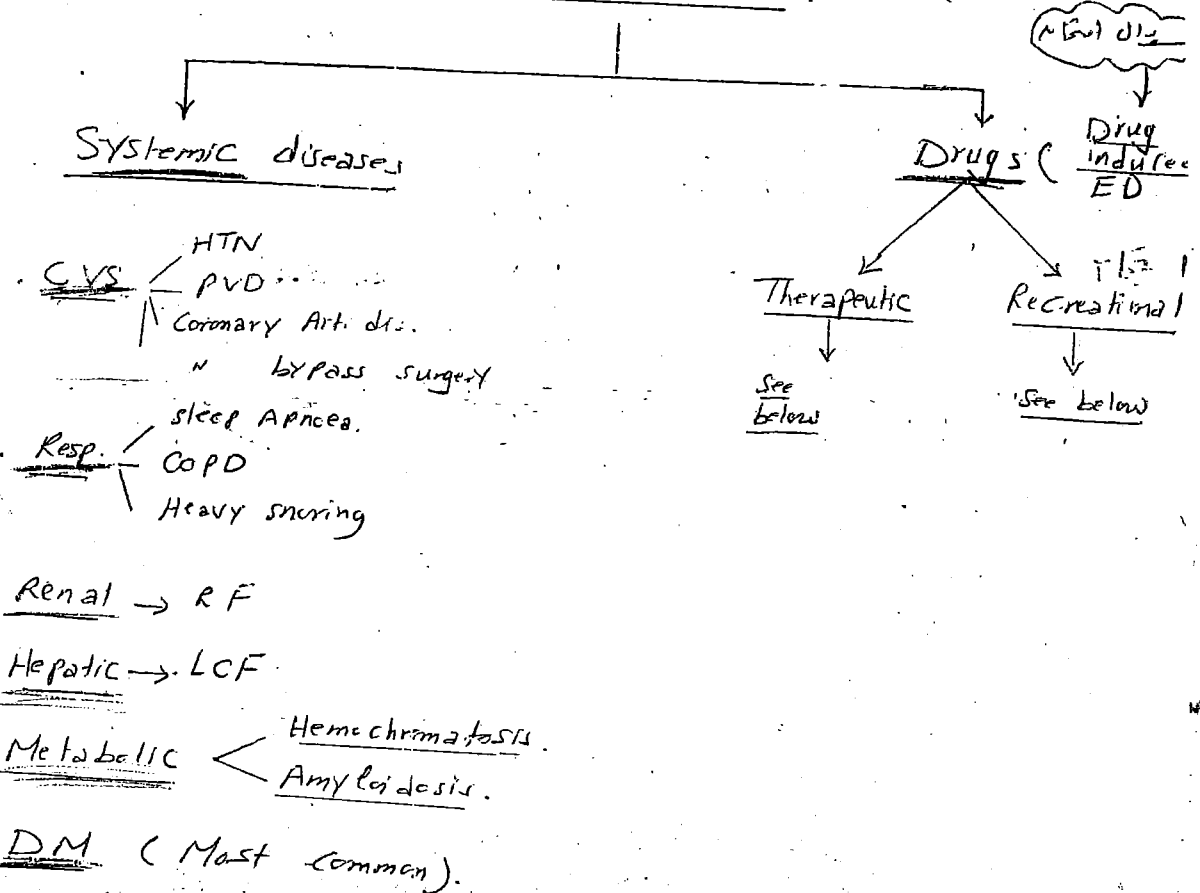
د. محمد صالح

— just print —

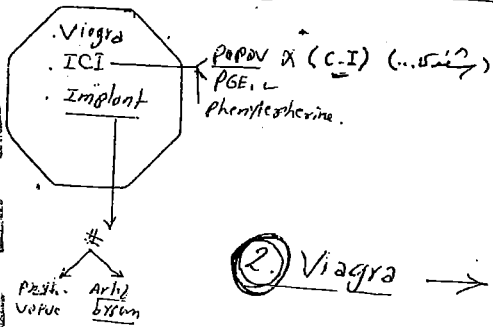
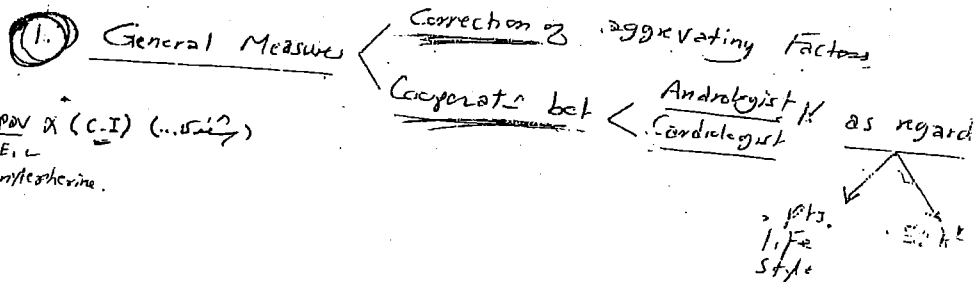
01025329200- 0502200362

# Medical Causes of ED

(80)



## Treatment



(2) Viagra → Get in patients e. Therapy for coronary Ht. dse → cause fetal hypotension

⑤ ICI:

- papaverine → better avoided d.t. its High Systemic absorpt. →
  - Hypotension
  - Vasovagal reflex (sp. if venogen. Inf.)

• Prostaglandin E<sub>1</sub> (Prostin VR):

- more safe when used in small doses (500) & occlusion of Penile base To avoid systemic pass.

- If There is prolonged Erection or Priapism → Vasconstrictors are RISKY

↓  
 X agonist ← phenylephrine (least Cardio-genic effect)  
 • Dopamine HCL

④ Penile prosthesis → Avoid it in pts. w/ adipocystic or valves ant. prosthesis

(d.t. risk of Hematogenous Inf. postoperatively.)

Sexual intercourse → prefer Female superior position

CV dis.   
 No papaverine  
 Small dose PG  
 if need Vasconstrictor → phenylephrine.  
 if take nitrate ≠ Viagra.

2 Respiratory diseases: <sup>Apnea</sup> ~~COPD~~ <sup>Snoring</sup>

sleep Apnea & Heavy Snoring → Arterial Hypoxia  
& Hypercapnia → pulm. & systemic HTN.

↓  
clear Association bet.  
ED & Sleep Apnea

COPD → ED in ~ 30%

3 Hepatic dis:

Chr. liver dis. ass. e ED in 50% of cases but incid. is ↑↑ to ~ 70%  
in cases of Alcoholic Cirrhosis.

<sup>50% ↑ PRL</sup> Mechanism: <sup>ELISA</sup>

- ↑ PRL prolactin
- ↑ SHBG
- ↑ Estrogen → -- LH → ↓ T.
- Alcoholic liver toxicity → Toxic effect on the axis (HPTA)

Q. # → PGE<sub>1</sub> → not safe.  
Papaverine → # (hepatic S.E).

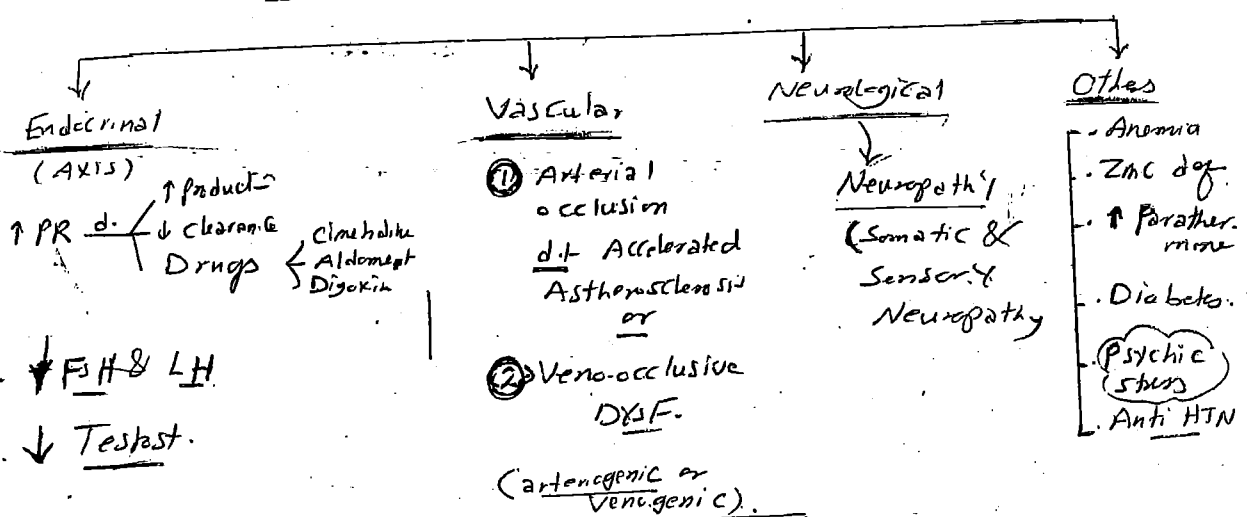
CLP  
- ↓ desire  
- GynecoMasbia  
- E.D



10/3

3 Renal diseases:  $\downarrow$  50% ED.  
 RF is assoc.  $\downarrow$  desire.  
 Infertility.

Mechanism:



Treatment

- ① Medical
  - Androgen Replacement.
  - Zinc supplementation.
  - PRL Inhibitory drugs.
  - Erythropoietin.
  - Viagra  $\rightarrow$  CL
- ② ICI
  - Effective
  - High dose  $e^-$  arterial dis.
  - Resistant in venogenic dis.
- ③ Penile Prosthesis: Best if ED persist after Renal Transplantation.
- ④ Renal Transplantation: Most efficient.
  - restore Erection in  $\approx 80\%$ .
  - persistent ED after Transplant.
  - is  $\downarrow$  ligate of Int. iliac during Transplant To be used for Anastomosis.

4 Metabolic

- ① Hemochromatosis:
  - Accumulation of Fe in Tissues.
  - Pituit. Tests.
  - D-M.
- ② Amylodosis:
  - Hereditary.
  - Type may involve the autonomic system.
  - $\rightarrow$  Neurogenic ED.
  - $\downarrow$  No specific HT.
  - (Cause of death is RF).

# Endocrinal ED

89

- ① Hypothalamic disorders
- ② pituitary disorders
- ③ Thyroid
- ④ Pancreatic → DM ✓
- ⑤ Adrenal
- ⑥ Testicular

1. Hypothalamic disorders → Hypogonadotropic Hypogonadism  
↓ GnRH, LH → ↓ testosterone  
↓ dose needed

## 2. Pituitary Causes

Hypogonadotropic Hypogonadism  
(↓ GnRH)

### Hyperprolactinemia

Mech.  $\left\{ \begin{array}{l} \text{-- GnRH} \rightarrow \downarrow T \\ \text{-- } 5\alpha \text{ reductase} \\ \text{direct effect on Testes (}\pm\text{)} \end{array} \right.$

clinically ED ass. with:  
↓ libido  
[ Gynecomastia ✓ ]

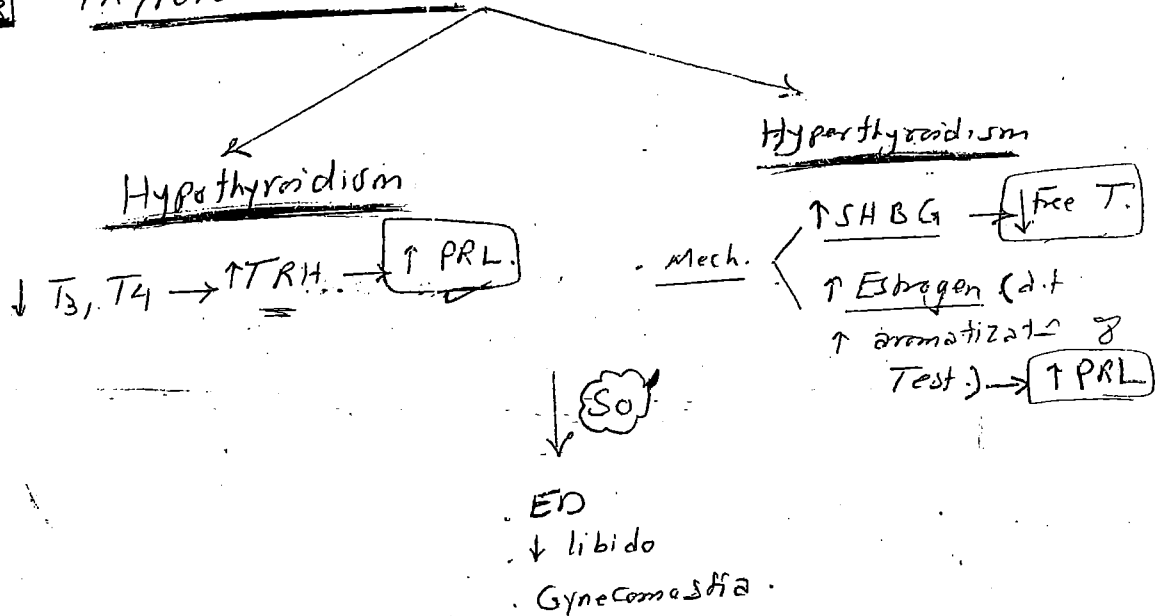
Causes → Sec infertility

NB



85

3

Thyroid disorders:

NB

NB

Hyperthyroidism & Androgen Resistance Synd.

2 Endocrinal causes of ED that not Ass. with  $\downarrow$  Test. This can be Explained

BY ① Hyperthyroidism :  $\rightarrow$  only Free T is  $\downarrow$ .

② ARS :  $\rightarrow$  receptor Resistance. ( $\uparrow$  T. level)

4

Pancreatic Causes

Diabetic Impotence (Spinal Nerve)

Insid - Commonest Endocrinological Cause of ED.

DM  $\uparrow$  3 times risk  $>$  NL

Diabetic at  $\rightarrow$  30%  $\rightarrow$  15% ED  
 $\rightarrow$  60%  $\rightarrow$  50% ED

- Risk groups
- ① old age
  - ② long duration
  - ③ Alcohol intake
  - ④ Neuropathy
  - ⑤ Retinopathy
  - ⑥ Intermittent claudication

# CIP (Types):

## Classical diabetic ED

- NL desire & Hormones
- Retrograde ejac. ±
- Noct. Erectn: ± Abnl despite of NL Sexual Erectn.
- Sexual Erection: gradual ↓ Rrigidity  
Followed by ↓ Freq. of Noct. Erectn.
- Psychogenic stress (performance anxiety)  
Convert it From Partial → complete;  
(Organic ED → psch. ED)
- Reversible in 8.5%

## Atypical (Acute) diabetic ED

- ass. with poor Control & Acute severe symptoms
- Hunger pain
- Thirst
- Wt loss
- Polyuria.

Reversible

## Pathogenesis

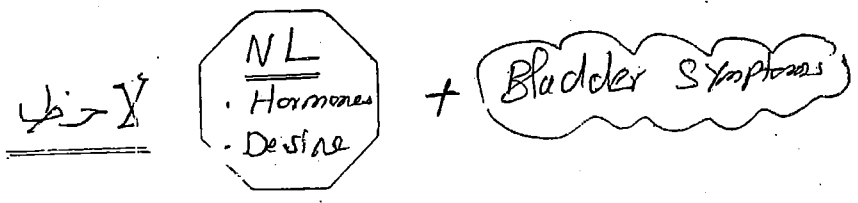
1. Neuropathy → autonomic & Somatic Neuropathy  
So usually ass. e Neuropathic Bladder  
Bladder dysfunction ← Retrograde EJ → d.t Common NS of Bladder & penis.

2. Vasculopathy →  
Microangiopathy: of small BV. → narrowing  
Arteriosclerosis: d.t ass HTN (lost elasticity)  
Atherosclerosis: d.t ass Hypercholesterolemia

3. Cavernous (Endothelial) .  $\downarrow$  Neurotransmitters  $\leftarrow$  VIP NO 87  
 $\uparrow$  ms. Tone  $\rightarrow$  weak erection

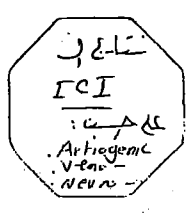
4. Metabolic Neurogenic Tissue Glycosylation  $\rightarrow$  ED

5. Psychogenic Partial ED  $\rightarrow$  Severe Performance  
Anxiety  $\rightarrow$  Complete ED.



Diagnosis of Diabetic ED:  $\rightarrow$  ICI, US, W1

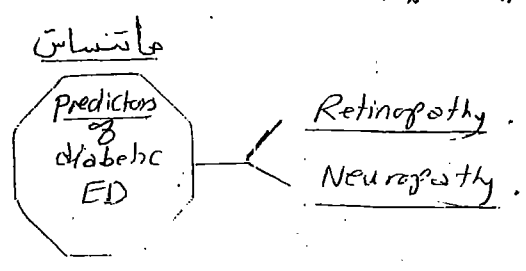
- ① History
- ② Exam.  $\rightarrow$  Neurological reflexes
- ③ Inv.



$\Delta$  Differentiation bet. organic & Psychogenic  $\leftarrow$  ICI  $\rightarrow$  Rigidity

$\Delta$  detection of cause  $\rightarrow$  organic.

- Inv. For Arterogenic
- " " Venous occlusive
- " " Neurogenic.



88

# Treatment

## Early stages

(Prevention is better than Control)

- ① strict diabetic control → ↓ progression of Neurologically micro-angiopathy
- ② Sex Therapy

↓ Anxiety & improve some pts.

## Late stage

1st line → non invasive HT (Viagra)

2nd line → ICI

3rd line → Implant

2 common S.E

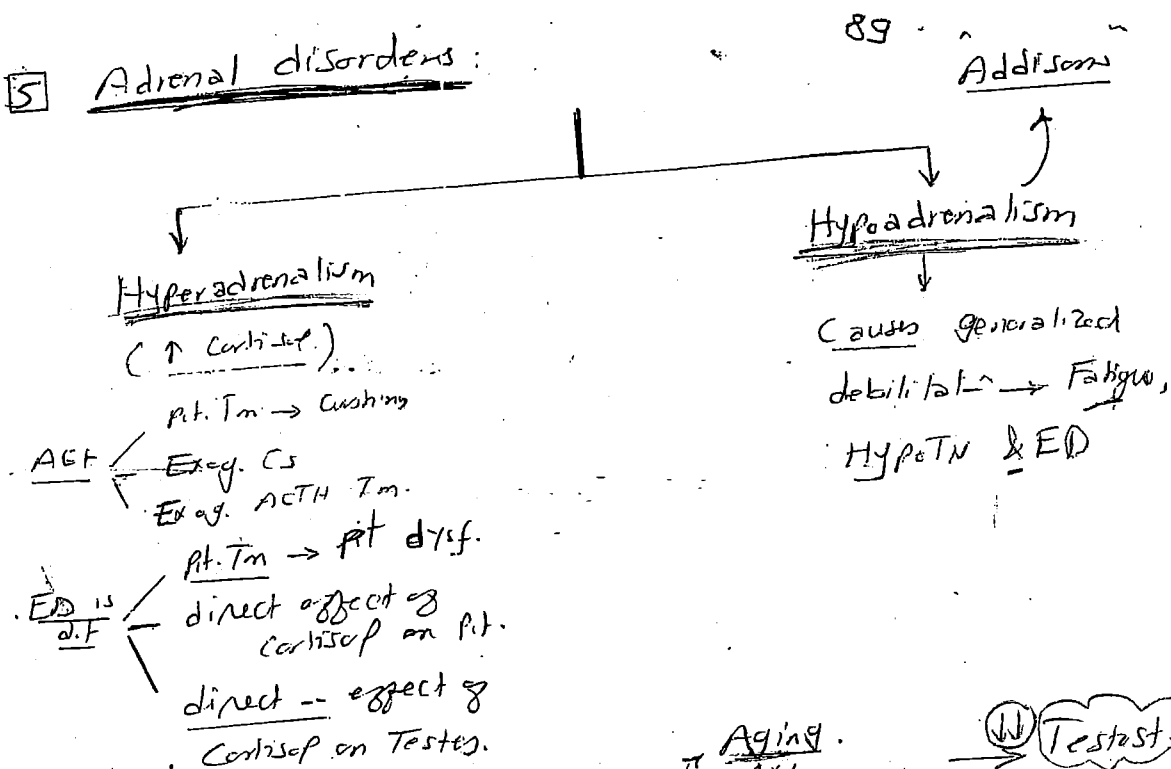
Inf.  
(avoided by)

Strict Aseptic Conditions

proper evaluation by Glycosylated Hb.

Erosion & Extrusion of the device avoided by avoiding too long devices.

## 5 Adrenal disorders:



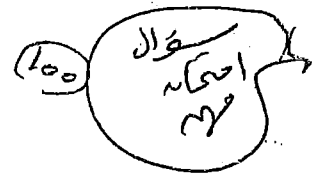
## 6 Testicular disorders:

- ... The basic rule... is that androgen replacement therapy is not effective in improving the sexual desire & performance except in patients with documented androgen deficiency
- Oral or injectable androgens aren't physiological ways in delivering androgens.
- New transdermal androgen delivery systems may be more physiological as they produce serum level similar to NL biological rhythms.

✓ Polychondria Autoimmune disease :- An Autoimmune disease that transmitted as an Autosomal dominant disease is Circulatory antibodies against many Endocrine glands → Multiple Endocrine Failure... Less common in males. In Addition to Testicular failure There may be Hypothyroidism, Hypo-Parathyroidism & I.D.M -- it has to diff. from panhypopituitarism.

سبب

## Iatrogenic ED



- ① Surgically <sup>& Trauma</sup> Induced ED
- ② Drug induced ED

### A. Surgically induced ED

#### 1. Arterogenic:

- Pelvic operation
  - Abd. operation
  - Pelvic Trauma & Irradiation
- } Antefemoral by pass  
- Iliofemoral by pass.  
Renal Transplant

Usually causes injury

↳ Int. pudendal → Common

Penile a. in pl. 20-40 x

### B. Venogenic ED:

• Priapism  
• Fracture  
• Lue II

Lue II - Abnormalities of Tunica Albuginea  
penile trauma

Lue III: Abnormalities of Cavernous smooth ms → Priapism

Lue IV: Abn. Acq. Venous Communication (Fistula)

Shunting operation for Priapism

- Trauma
- Transurethral Surgery



(C) Neurogenic ED:

Brain → Trauma

Spinal Cord → Disc  
SCI

peripheral Nerve injury:

operation:  $\left\{ \begin{array}{l} \text{UR} \\ \text{prostate} \\ \text{urethra} \end{array} \right.$

pelvic fracture

TORP

(D) Penile Cause of Intragenic ED:

Excision  
of  
plaque

Pyrexia's d.t. trauma by  $\left\{ \begin{array}{l} \text{ICI} \\ \text{VCD} \\ \text{Sexual interC.} \end{array} \right.$

It may → ED

Priapism

Pelvic

$\left\{ \begin{array}{l} \text{Edema} \\ \text{Hemorrhage} \\ \text{Metastases of penis} \end{array} \right. \rightarrow \text{obstr. Venous}$

Surgical shunting

Venogenic ED

(E) Endocrinological Cause:

Trauma or operation

to  $\left\{ \begin{array}{l} \text{Hypoth} \\ \text{Pit.} \\ \text{Testes} \\ \text{Suprarenal} \\ \text{Thyroid} \end{array} \right.$

drugs

(F) Medical Cause

## 7. Hormones

• Oestrogens  
(in H<sub>2</sub> Cancer Prost.)

↓ Libido.

• GnRH Inhibitors:  
Leuprolide.

## Antiandrogens

- Cimetidine (++)
- Ranitidine (+)
- Famotidine (No)
- Aldactone
- Ketoconazole
- Cypionate acetate (Danu)

(99) Flutamide

New Anti-androgen with effect on Libido or Prolactin

## 8. Recreational Drugs

### A. Alcohol

#### Acute effects

- Small dose
  - ↑ desire (d.t. Release from inhibition)
- Large dose
  - acute ED (d.t. central inhibition of dopaminergic system)

#### Chr. effects

- ED
- ↓ Libido
- Gynaecomastia
- ejac. disturb.

why { CNS depression  
neuropathy  
↑ PR  
direct effect on testic. func.  
LCF → Testis - Steroids

### B. Marijuana, Cocaine, Heroin:

- ↓ Test.
- ↓ Libido
- Gynaecomastia
- ED

### C. Smoking

## 9. Other Drugs

#### Acute effects

acute VC & disturbance in Veno-occlusive Mechanism of Corp. Cav.

ICI (in M<sub>2</sub>, L<sub>2</sub>)  
↓  
(Failed test)

#### Chr. Effects

- Inverse relation bet. No. of Cigarettes & rigidity & duration of noct. Erect.
- ↑ Risk if
  - Aging
  - DM
  - HD

• Digoxine: Similar in its structure to sex steroids.

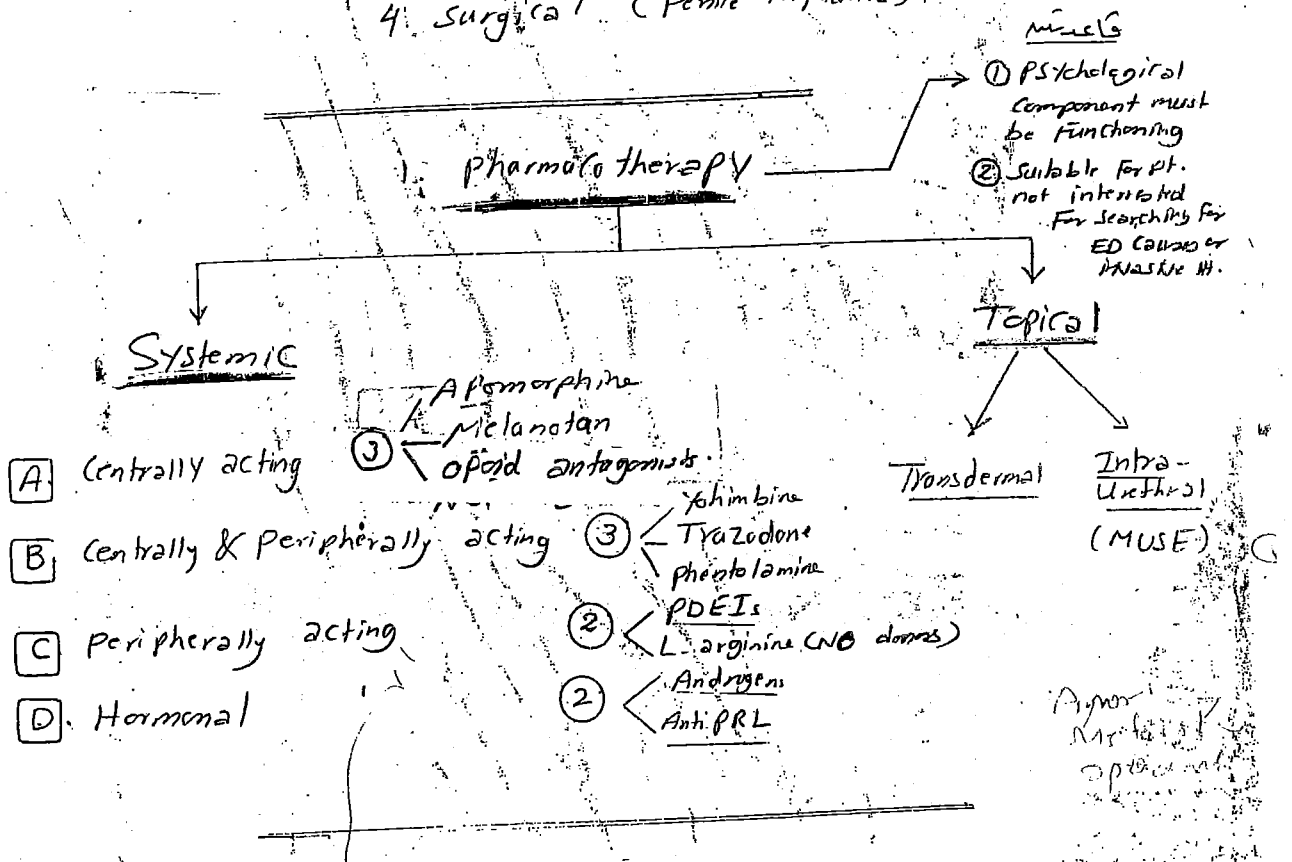
- ↓ T
- ↑ PRL
- ↑ Estrogen

- NSAIDs
- Metronidazole.
- Cytotoxics — MTX cyclophosphamide
- Clofibrate. (Anti Hyper-lipidemic)



# Treatment of ED

1. Pharmacotherapy Systemic  
Topical
2. ICI
3. VED
4. Surgical (Penile Implants)



## ① Apomorphine (Uprima®)

Mechanism → Dopamine Agonist (↑↑ D<sub>2</sub> R<sub>s</sub> in Hypothalamus)

Dose: 4-6 mg Sublingual (oral not effective)

Effect: Success Response (70%)

promise to become most effective H

For ED: Test & No dependant  
(Specially PSCs)

Nausea ✓

Vomiting ✓

Yawning ✓

S.E

③ ② Melanotan II (Palatin)<sup>®</sup>



Mech. → Melanocortin Rs. Agonist (has Melanocortins like action)

Melanocortins  $\leftarrow$   $\alpha$  MSH.  
Adrenocorticotrophic (ACTH)

Both regulate Sexual behaviour & motivation Ects.

acts mainly on MCs 3 & 4.

Contraindications → Efficacy:  $\uparrow$  desire  
 $\uparrow$  Erection.

③ Nalhexone:

H of resistant Hepatic priapism & Renal

Mech. → Opiates Antagonist

Note Opiates --  $\leftarrow$  Sexual drive.  
" performance.  
GnRH

Efficacy: Some studies supported its efficacy in improving Erection in Idiopathic ED. while other studies didn't support But in both studies it ( $\uparrow$  NPT.)

Recommendation: used in ED  $\bar{c}$  altered Central opioid tone.

④ Nalmefene:

Mechanism: long acting opioid Antagonist (derived from Nalhexone)  $\rightarrow$  (++ Axis) activity  
 $\rightarrow$  ( $\uparrow$  LH, FSH & T) (but no change in NPT)

## 1. Centrally & Peripherally Acting

### 1. Yohimbine

Mech. ①  $\alpha_2$  Blocker  $\left\{ \begin{array}{l} \text{Centrally} \rightarrow \text{Excit.} \\ \text{peripherally} \rightarrow \text{Relaxation} \end{array} \right. \rightarrow \text{vascular \& corporal smooth m.}$

②.  $\uparrow$  eNO.

③.  $++$  desire  $\rightarrow$   $\sim$  aphrodisiac Effect

dose: 10 mg three times / day. [30 mg M]

(4) (عند)

Centrally  
peripherally  
eNO  
++ desire

طريقة الإستعمال:  $\Delta$  on demand  $\leftarrow$  قبل الحاجة إليه

Continuous  $\Delta$   $\leftarrow$  يستعمل يوميا (دائما)

انه لا يرفع ضغطه لولا ان له اثار جانبية  
كبيرة (كوسيلة)

Improvement  
erection with  
mainly in psychogenic ED

في البروستاتا

يعطى في  
كبسولة  
او قرص

Tritico tab.

S.E

Headache.  
Insomnia.

Tremors  
palpitation

HTN. (marginal  $\uparrow$  in diastolic).

لا يرفع ضغطه

serotonin  $\rightarrow$   
sexual fun.

### 2. Trazodone (Tritico $\leftarrow$ 50 tab) $\Delta$

Non TCA Serotonin  $\times$  Reuptake inhibitor.  $\Delta$  Antagonist &  $\Delta$  class of antidepressant

Mech. Exact mechanism is unknown (but)  $\Delta$   $\leftarrow$  centrally  $\rightarrow$  Serotonin Antagonist  $\rightarrow$   $\downarrow$  Excit.  $\rightarrow$  depressant

$\left\{ \begin{array}{l} \text{Centrally} \rightarrow \text{Serotonin Antagonist} \rightarrow \downarrow \text{Excit.} \\ \text{Peripherally} \rightarrow \alpha \text{ blocker} \rightarrow \text{Sympatholytic} \rightarrow \text{Excit.} \\ \text{Serotonin Antagonist} \rightarrow \text{Excit.} \end{array} \right.$

dose: 50-100 mg/d

- S.E:
- sedation
  - orthostatic HypoTN
  - Priapism

Efficacy: (Controversy):

- success rate 60%
- good in pt. w/ ED + Anxiety or depression  
Serotonin syndrome
- Recent study  $\rightarrow$  Not effective.

Note Tritico  $\left\{ \begin{array}{l} \text{large dose} \rightarrow -- \text{Erecta (Serotonin Agonist)} \\ \text{small dose} \rightarrow ++ \text{Erecta (}\alpha\text{-Blocker)} \end{array} \right.$   
Serotonin Antagonist.

### 3. Phentolamine (Vasomax):

$\alpha$  Blockers ( $\alpha_1$  &  $\alpha_2$ )  $\rightarrow$  sympatholytic  $\rightarrow$   $++$  erection

dose: 50-100 mg/d at bed time

- S.E:
- [ HypoTN
  - [ Nausea
  - [ Vomiting
  - [ drowsiness
  - [ lethargy

☒ Peripherally Acting pDEs

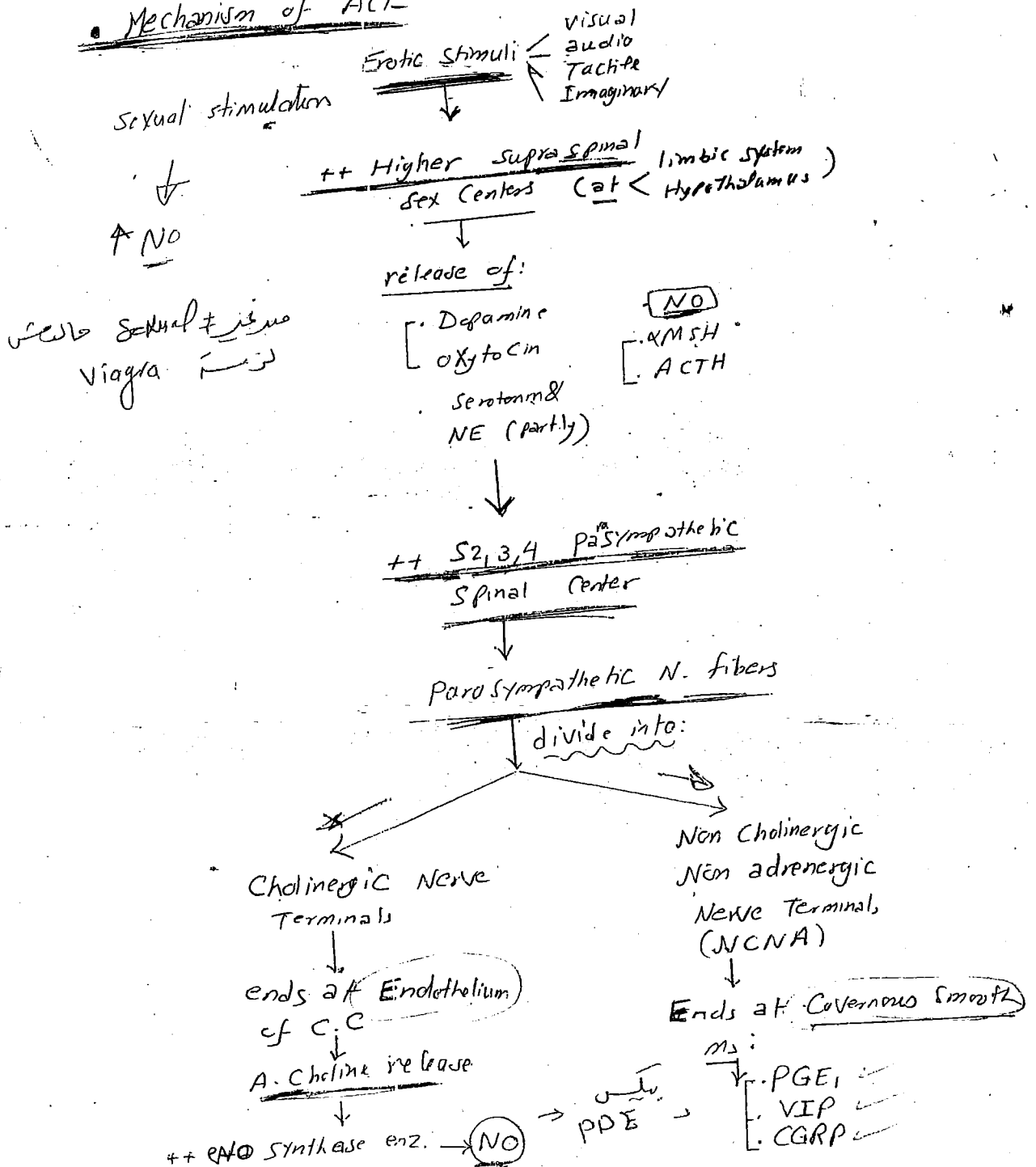
- ✓ ①. PDE Is  $\left\{ \begin{array}{l} \text{Selective} \\ \text{Non selective} \end{array} \right.$
- ②. NO donor (L-arginine)

# I. Selective phosphodiesterase Inhibitors:

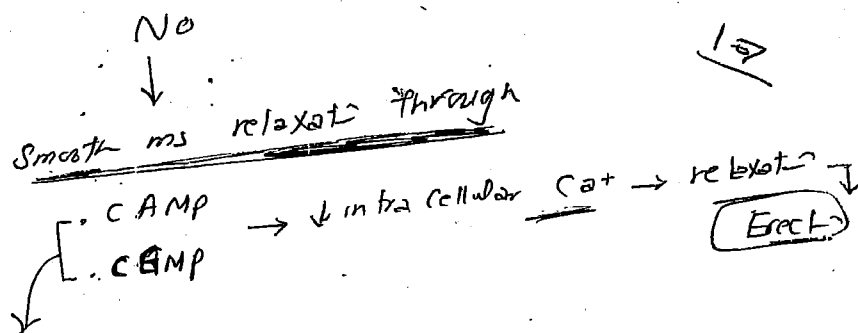
1. Sildenafil [Viagra] ®
2. Tadalafil [Cialis] ®
3. Vardenafil [Levitra] ®

105

## Mechanism of Action







these are the Active 2nd Messengers in Smooth ms. relaxat<sup>n</sup> & Erect<sup>n</sup>.

They are inactivated (destroyed) by PDE

**PDE enz** has Main 11 Iso forms:  
 → PDE 1, 2, 3, 10, 11 → -- cAMP & cGMP  
 → PDE 4, 7, 8 → -- cAMP  
 → PDE 5, 6, 9 → -- cGMP

**PDEs present in:**  
 ① penis inhib<sup>n</sup> of ED  
 ② Lung → Inhib<sup>n</sup> of pulm. HTN.

**Viagra** is a selective PDE5 inhibitor →  
 ↑ cGMP → Erect<sup>n</sup> in retina

also weak PDE6-I → ocular S.E.

Pharmacokinetics & Dose

50-200 mg 1 before coitus by ~ empty stomach  
 0.5-4 hrs (average 1 hr) →  
 onset of act<sup>n</sup> is 20 min [Maximum 0.5-2 hrs] → act<sup>n</sup> that may extend for up to ≥ 24 hrs.

Duration of Efficacy 4 hrs. U-6

| PDE5 Inhibitors   |                                    |  |
|---|------------------------------------|--|
| Not to take if you are on the PDE5 inhibitors. The PDE5 inhibitors are not to be taken with nitrates. Do not take if you are on the PDE5 inhibitors. The PDE5 inhibitors are not to be taken with nitrates. |                                    |  |
| Onset of action   | Onset of action                    | Onset of action                            |
| 20-60 minutes   | 20-60 minutes                      | 20-60 minutes                              |
| Length of action  | Length of action                   | Length of action                           |
| 24-36 hours   | 2 hours (??)                       | 4-6 hours                                  |
| Efficacy  | Efficacy                           | Efficacy                                   |
| 70-80%  | 70-80%                             | 70-80%                                     |
| Points to consider  | Points to consider                 | Points to consider                         |
| Meals do not affect absorption  | A fatty meal may affect absorption | Repeat and heavy meals may slow absorption |

108

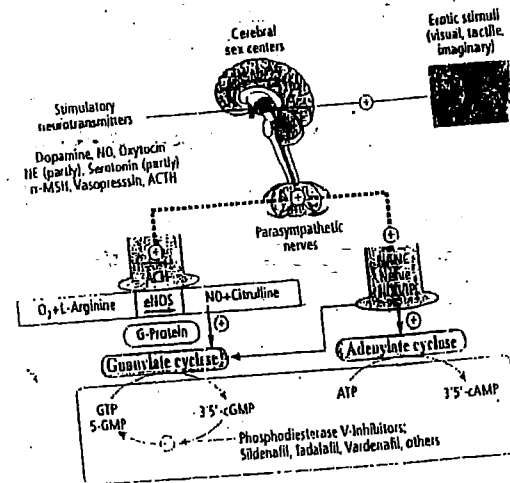


Fig. 18.1: Physiology of erection and the impact of PDE inhibitors

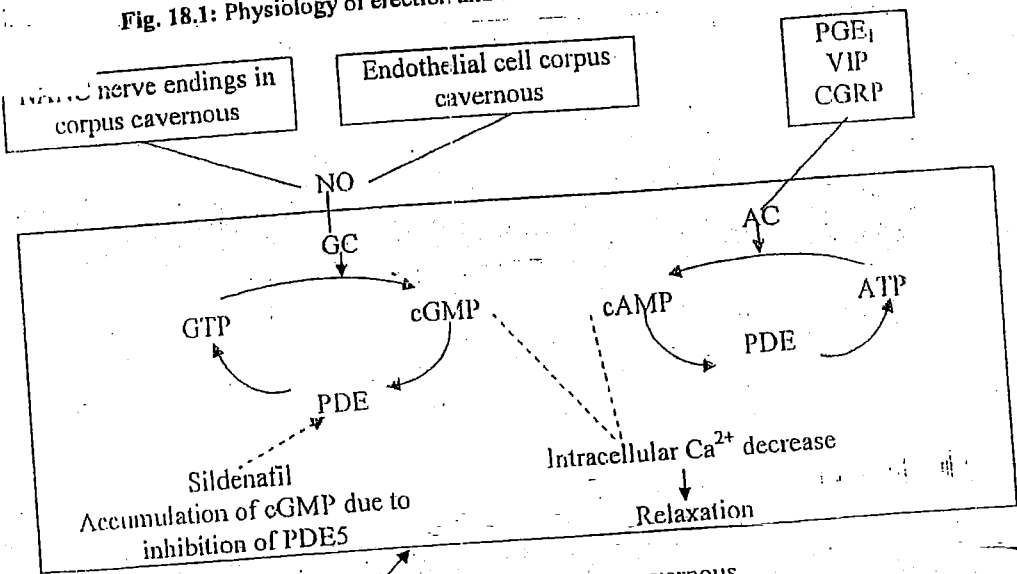


Fig. 18.2: Cellular mechanism of erection in the cavernous smooth muscle cell.

Kine HS

Rapid absorption after oral intake. ✓  
conc. (30-120 mins)

Rapid absorption Maximal plasma conc. (30-120 mins)  
Excreted in feces

(Fatty acid  $\downarrow$  extend  
cg Abs. by 29%)

- Metabolized in liver & Excreted in feces (80%)  
urine (13%)

Larva (13%)

109

Pix  
Empty  
Stomach  
an.

بسم الله الرحمن الرحيم  
أو ضل عن  
بأمة

Therapeutic effects:

therapeutic effects:

(1) sild. is Erection Enhancer rather than erection Inducer (not aphrodisiac; so sexual excitation required).

↓  
(یعنی)  
No طبعان

7  
عشمان رطلع (عقودت) ۲۰

## ② Efficacy in different conditions:

✓ (21) NL individuals → no effect on ered  
ED → 88% (c. Regular U)

(14). NL individuals → no effect in exercise  
(15). Psychogenic ED → 88% (regular use) & 92% (on demand use)  
placebo was (38%)  
placebo was (27%)

©. organic ED → obvious but < psychogenic.

(d). Mixed org. & psychog. → 78% (placebo 29%)

④. SCI → 65-80%

(E) SCI  $\rightarrow$  85-80%  
 (F) Diabetic  $\rightarrow$  57% (placebo 10%)  
 43%

⑧. Radical prostatectomy → 43%

(So it is the most effective & promising drug  
in treatment of ED.)

S.E  $\rightarrow$  Few  
Higher doses (100-200 mg)  
rarely requires stop of the drug.

• direct effect of  
-- PDEs in VD  
tissues

- ① Headache
- ② Facial Flushing
- ③ Dyspepsia

(A)  
~~Common~~  
not-serious

(B) Rare but  
serious

- ① Prismatic
- ② severe hypoxia.
- ③ M.I
- ④ arrhythmia
- ⑤ stroke
- ⑥ visual impairment  
(NATION)

⑤ Visual Disturbances

Some uses  
ex postmorta  
these so  
FDA 2005  
Alert

- ✓ (a) blurring
- ✓ (b) loss of peripheral vision
- ✓ (c) color blindness
- ✓ (d) ↑ IOP intraocular pressure.

✓ <sup>PDX</sup> ② Nonaromatic Ant. Isch  
optic Neurog. Aky  
(Sugg. by many stu)

## Contra Indications:

1. Hypersensitivity to it.

2. Pls Receiving Nitrates (organic nitrates & No donors)  
TCAM → V.D, Synergism  
Viagra → Fatal Hypotension & Arrhythmia

24 hrs (in Solid.)  
48 hrs (in Vard) ↓  
d.t. prolonged half life

3. Retinitis pigmentosa  
(Hereditary degenerative retinal disorder)

4. Others → Severe hepatic impairment  
Renal  
Recent stroke or Heart attack.

## Drug interactions:

Never given to patients taken Nitroglycerine or isosorbide

Cytochrome P 450 inhibitors as: Metabolize Viagra.  
Erythromycin  
Ketoconazole  
Itraconazole  
Cimetidine  
↓ Clearance of Viagra & potentiate its effect

protease inhibitors →  
-- Viagra Metabolism level.

we're HIV  
Tadalafil (Cialis)

(FDA approved for Lilly at April 2002).

changes in Viagra in: more potent

1) greater selectivity. on PDE5 only

2) longer duration of act (upto 36 hrs) → So called Weekend Pill.

3) dose 10-20 mg/d

4) Safer than Viagra

5) S.E → as Viagra but

Back pain ++ or Myalgia  
No Visual disturbances.

6) No interaction food

(No interaction with food)

1) Eye less than Viagra, Tadalafil & Levitra

Called: non Arteritic ant. ischemic optic neuropathy (NAION)  
→ Block of Blood Flow to optic N.

High Risk Zone: 1) Heart dis  
2) > 50

3) Diabetic  
4) HTN

5) smoker  
6) T. cholest.  
7) Eye problems

FDA alert in  
7/2005

112

## Vardenafil (Levitra)<sup>R</sup>

(Bayer)

P. 24

onset  
↓  
Vardenafil  
> Viagra  
> Tadalafil

- differs from Viagra
- ① More potent & more selective on PDE5
  - ② More safe
  - ③ dose: 10-20mg
  - ④ half life 8 hr [duration of efficacy 8+?]
  - ⑤ S.E → ...

### Other uses of PDEIs:

1. Pyrexia dis.
2. prevention of stuttering priapism.
3. Raynaud's phenomenon
4. Pulmonary HTN.
5. premature ejaculation

### ①. Non-selective Phosphodiesterase

Trental ⇒ Inhibitors (Pentoxifylline)

1-2g/d (or)  
1200mg/d  
For 2wks

- some pts receiving it for ischemia showed improved sexual function by VD
- the studies: showed its effectiveness.

Mechanism

- ↓ viscosity
- ↑ RBCs flexibility ++
- ↑ peripheral flow

### ② No donors (L. arginine)

2 studies

- 2800 mg/d For 2wks → improve 40% [only on those with low level of ...]
- 5000 mg/d For 6wks → 31% (No)
- check ...

Good response if combined with Yohimbine

(NB)

Gonotrex = Fish Roe + Ginkgo-biloba extract → improve sexual desire & ↑ blood flow.

L. arginine → No

## D. Hormonal HT

### ① Androgen therapy

#### indications:

- ↓ libido
- Severe Hypogonadism
- Adjuvant HT when other drugs are unsuccessful by them selves.

Mech.

- ↑ libido & sense of well being
- improve penile vascularity.
- regulate PDE5 activity (dil.).

(HL)

in Recent study: Pt.  $\bar{e}$  low or low NL T level who Failed response to PDEIs (Vigra = PDEIs non responder) → TRT give +ve results.  
(So altered level may alter PDE5 Expression)

Supraphysiological level of T

- may:
- ↑ desire
  - No effect in Frequency of sex.

(X) threshold for this alteration is: (HL)

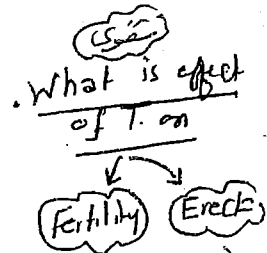
- Total:  $\leq 10-13$  nmol/L
- Free:  $\leq 200-250$  pmol/L

Forms & doses → See TRT

### ② Antiprolactin:

Hyper Prolactinemia is ass. e:

- ED
- ↓ libido
- Gynecomastia
- Hypogonadism.



# Phosphodiesterase (PDE) System

1/2

Number: 11 families & total Number of > 50 isoforms.

Function: acting on the second Messengers  $\begin{cases} \text{cAMP} \\ \text{cGMP} \end{cases}$

→ hydrolyze the phosphodiesterase bond →

breakdown of  $\begin{cases} \text{cAMP} \xrightarrow{\text{to}} \text{cATP} \\ \text{cGMP} \xrightarrow{\text{to}} \text{cGMP} \end{cases}$  [biologically inactive Monophosphates]

→ ↑ Intracellular Cat →

Smooth ms. Contract → Flaccidity.

Sites: Heart, Lung, Kidney, Retina, Vascular & Visceral Smooth ms, Testis & ovary.

What are Types of PDE present in Cavernous Tissue??

• PDEs → most abundant

• Other Types:

• PDE1:  $\begin{cases} A \\ B \\ C \end{cases}$

• PDE2: A

• PDE3: A

• PDE4: A, B, C, D

• PDE  $\begin{cases} 7A \\ 8A \\ 9A \\ 10A \end{cases}$

[also present in  $\begin{cases} \text{CVS} \\ \text{CNS} \\ \text{Vasculum} \\ \text{S.m.} \end{cases}$  → Headache, Clonidine, Tachycardia]

MEPL  
6 types

• PDE4 & 5 inhibitors: -- Migrate & prolif. of smooth m.

• PDE3 & 4 inhibitors: ↓ restenosis after angioplasty procedures (So) They are undertrial for their potential Angiogenic effects.

# PDE-I

معدلات استجابة  
للمرضى

45

## on demand use

قبل الجماع (الاستجابة)

20 mg before act.

1/2 - 4 h

not E- 20 mg

for 4 h

## Chronic daily dosing

ليومياً

adv.

### ① Effective in the following Conditions:

- PDE-I Non responders.
- Sexual rehabilitat<sup>n</sup> of pls. after Nerve sparing radical prostatectomy.
- EDE CV risk Factors.

### ② Improves Endothelial dysfunction (of C.C & all body endoth.)

### ③ Improving voiding difficulties in BP pt (as PDEs are widely distributed in prostate)

### ④ relieves the patient from scheduling sexual activities.

Male

## PDE-I Non responders:

Definition of them: [real non responders]

### Failure of response to PDE-I under the following conditions:

- ① Use of at least 4 tablets of highest dose M<sup>at</sup>-dose.
- ② At 4 different occasions.
- ③ Under optimal conditions & appropriate Sexual stim.

توصى وقتاً مناسباً بعد الإفطار (Viagra & Varden) ويبدأ الجماع  
أولاً وقتاً مناسباً بعد تناول (Tadalafil) ويبدأ الجماع (موصى به أيضاً)



• The overcome this problem; Measures  
That can be done are:

① Use High dose → doubling the <sup>400</sup> Maximum dose.

② Shifting to another Type of PDE5I: From Sildenafil to Vardenafil

③ Daily Dosing:

④ Treatment of Concomitant

(A) Hypogonadism : Testosterone

[ PDE-I non responders ]  
⊕ a Sign of Hypogonadism

regulates PDE-5  
expression  
regulates PDE-5  
responsiveness to  
the inhibitors.  
Cavernous VP.

(B) HTN, Hypercholesterolemia & DM.

Comparison  
bet  
PGE1 &  
Sildenafil

| PGE1  | Sildenafil     |
|---|----------------|
| ✓ Invasive  | • non-Invasive |
| ✓ No. need for sexual<br>stim.                      | • Needed       |
| • Erection onset: 10-15 min.                        | • 60 min.      |
| ✓ Mech. ↑ cAMP                                      | • ↑ cGMP       |
| • Type of Erec: Induced<br>(non physiology)<br>(ca) | • Spontaneous  |
| ✓ Use in ED: 2nd<br>line.                           | • 1st line.    |

NB Newer PDE5I → (161)

# Topical pharmacotherapy

- A. Transdermal
- B. Intra Urethral (MUSE)

## A. Transdermal

- ① Nitroglycerine
- ② Minoxidil
- ③ papaverine

### ① Nitroglycerine:

Mechanism → Release NO.

→ binds to Guanylate

Cyclase System → cGMP → ...

muscle Relaxat<sup>n</sup> = erection

used as 2% < oint / patch to penis & perineum.

studies ① improve erection  
(but) not rigidity

② better in pts w<sup>th</sup> SCI

Limitat<sup>n</sup>: poor absorption through the thick tunica →

Some make window in Buck's fascia & Tunica Albuginea & cover it w<sup>th</sup> graft from deep dorsal vein & oint. applied over skin

S.E: Headach & Hypotension in both partners.

### ② Minoxidil:

Mech. → K Channel opener →

Ca entry inside cells

→ Relaxat<sup>n</sup> & penis erect

used as: .1ml, 2% sol. (capsicum)

Better when: Combined w<sup>th</sup> Capsicum

→ enhance Abs.

### ③ Papaverine gel (15-20%) →

improve ED (in) SCI Cases

PDEI & cAMP

Alprostadil

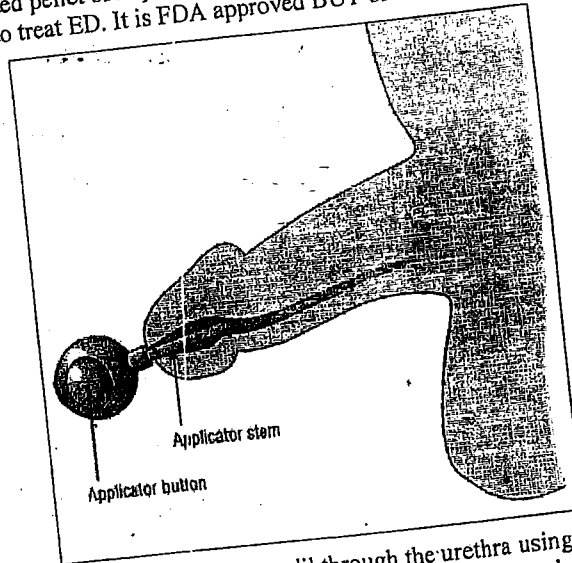
78

p. 30

B intraurethral

MEDICATED URETHRAL SYSTEM FOR ERECTION  
(MUSE)

MUSE is short for "medicated urethral system for erection." It consists of a tiny medicated pellet of Alprostadil (prostaglandin E1) that is inserted into the urethra to treat ED. It is FDA approved BUT of controversial results.



Administration of the drug alprostadil through the urethra using the MUSE system is an effective alternative treatment for many men, and provides a less invasive alternative to intrapenile injection.

Alprostadil is a prostaglandin E preparation in a pellet form that is inserted with a plunger-like mechanism into the urethral opening. The plunger device is a thin plastic tube with a button at the top.



Mechanism: through delivering PGE1 into the urethra mucosa (good absorption in contrast to poor absorption through tunica) → absorption to C. spongiosum then to C. cavernosum (due to venous communication between them).

What is mechanism of PGE1 (مکتب)

4 CAMP → ↓ intracell  
Ca  
→ relaxation

Apparatus: Formed of 2 parts.

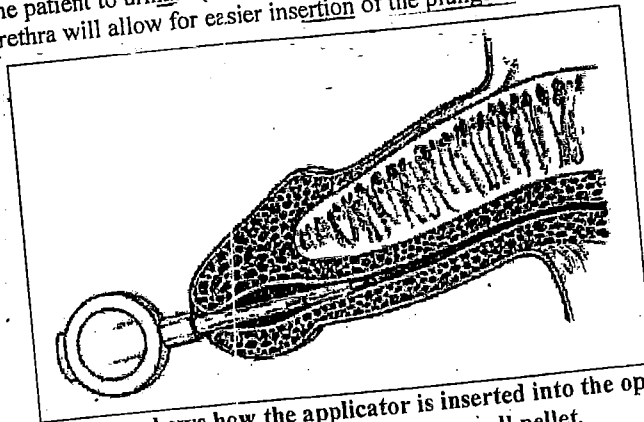
② plastic tube.

**A. Plunger (المكبس)**

The plunger device is pre-filled to deliver a pellet about an inch deep into the urethra at the tip of the penis.

**Method:**

- \* Using a plunger device, PGE1 is inserted into the urethral opening. The plunger device is a thin plastic tube with a button at the top.
- \* Ask the patient to urinate (because lubricants should not be used and a moist urethra will allow for easier insertion of the plunger device).



This illustration shows how the applicator is inserted into the opening at the end of the penis to leave the small pellet.

- \* Insert the tube about 1 inch into the urethral opening and press the button → A pellet containing the drug is released.

- \* After insertion, the pellet within the urethra should be dissolved by massaging or "kneading" the penis for about a minute.

- \* To avoid discomfort, keep the penis as straight as possible during administration. Roll the penis between his hands for 0 to 30 seconds to evenly distribute the drug.

- \* Avoid Urinating or urine leakage right after administration (may reduce the amount of medication).

- \* the patient is asked to get upright (either sitting, standing or walking for about 10 minutes after administration, If you lie on your back too soon after administration, blood flow to the penis may decrease and the erection may be lost).

- \* Erection will be achieved that lasts between 30 to 60 minutes. The erection may continue after orgasm.

**Dose:** Start is 500 µg & then either ↑ or ↓  
The dose according to the response.

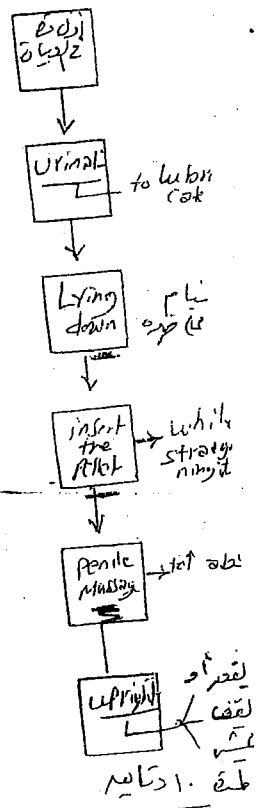
Not ≥ 1-2 times/day.

**SE:** ① Pain (testicular or penile)

② Burning sensation & Bleeding

③ Hypotension

④ SE of PGE → priapism or fibrosis.



120

NB: IF significant symptoms of hypotension Symptoms include dizziness, lightheadedness, and fainting. If these symptoms occur, the man should lie down immediately with his legs raised.

⑤ Female SE: \*Vaginal burning or itching OR TOXIC EFFECT ON FETUS (if she is pregnant)

\* One of the more unusual side effects involved a case where the MUSE pellet became caught in a female partner's mouth during oral sex and created an allergic reaction which necessitated a trip to the emergency room. For this reason, oral sex is not recommended when using the MUSE system..

#### Contra-Indications:

- ① Blood coagulopathy or using anticoagulants.
- ② if the female is pregnant or is likely to get pregnant (use condom)
- ③ hypersensitivity to prostaglandin, and sickle cell anemia.
- ④ Abnormal penial anatomy
- ⑤ Taking certain cold and allergy remedies may offset the effects of the MUSE-administered drug

teratogenic

#### Efficacy (علاج)

The Medicated Urethral System for Erection study group - (M.U.S.E.) have mentioned good results with the use of transurethral alprostadil, in a pioneer study; 64,9% of patients had sexual intercourse at home, regardless of impotence etiology and their age, with only 5,1% of discreet urethral traumas. However, 32,7% of the patients mentioned pain after the transurethral application. More recently, Porst reported that 43% of patients treated with 1000mcg of transurethral alprostadil were able to have a sexual intercourse, but only 10% mentioned rigid erection. Similarly, Werthman and Rajfer obtained 30% of erections that enabled vaginal penetration, but only 7% of 100 patients using up to 1000mcg of alprostadil mentioned rigid erections.

In another study, the efficacy of intraurethral alprostadil was evaluated in a double-blind, placebo-controlled trial in 1511 men with chronic erectile dysfunction from a variety of organic causes. Two-third of these men responded to intraurethral alprostadil with an erection sufficient for intercourse in the clinic; these men were then randomly assigned to therapy with either alprostadil or placebo. Successful intercourse on at least one occasion was much more likely with alprostadil (65 versus 19 percent with placebo). Among the men who responded to alprostadil, 7 of 10 applications were followed by successful intercourse.

\* In one study, 65% of men achieved erection using MUSE, and these men achieved intercourse in an average of 7 out of 10 administrations. A more recent study, however, reported disappointing results, with only 27% achieving erections and only 18% requesting additional refills.

ICI

ICI  
(IntraCavernosal = IntraCorporal inject-)

"Def. -

Diagnostic & therapeutic method for ED / based on direct  
injection of drugs into Corpora Cavernosa.

there are 3 main Drugs used:

|                             | Papaverine                                     | Phentolamine  | Prostaglandin E <sub>1</sub> (PGE <sub>1</sub> )  |
|-----------------------------|--|---|---|
| <u>Mechanism</u>            | Non selective PDE <sub>4</sub> → ↑ cAMP & cGMP | α Blocker → relaxat <sup>n</sup> (α <sub>1</sub> & α <sub>2</sub> ) | (1) ++ Adenyl cyclase → ↑ cAMP<br>(2) -- Collagenase (TGFS) enz. (No fibrinol)<br>(3) -- platelet aggregat <sup>n</sup> |
| <u>Half life</u>            | 1-2 hrs  | 0.5 hr<br>30 min  | < 1 min   |
| <u>Metabolism</u>           | by liver                                       | Extensive <sup>Metab.</sup> Metab. before exc.                      | 90% Metabolized in a single pass through <u>lung</u> .  |
| <u>Preparat<sup>n</sup></u> | "Papaverine"<br>الابيدال من فيه 7.6 جم         | "Rigitin" (R)<br>الابيدال من فيه 1.6 جم                             | Alprostadil (R)<br>Caverject (R)<br>الابيدال من فيه 0.5 مل  |
| <u>S.E / Adv.</u><br>(main) | Fibrosis <sup>Peyronie's</sup>                 | Tumescence (not rigidity)   | Pain  |
| <u>(disadv)</u>             | Priapism<br>Hypotension                        | Hypotension<br>Tachycardia  | less common<br>Fibrosis   |

NB:

FDA approved.

• Andropen:

Autoinjection device

• Other less commonly used drugs: لا شائعة  
فعلياً.

- CGRP
- VIP
- Na-Nitroprusside

Dose & preparations: 1. When using Single Agent:-

• Papaverine: 30-120 mg (usually 30-60)  
• Phentolamine: 0.5-1 mg  
• PGE: 10-20 µg.

2. Using Combination:-

**Bimex** تولمين

Rigith + Papaverine (1:30)  
(1 mg) + (30 mg)

↓  
prapism

NB phentolamine +  
replaced by  
chlorpromazine.

**Trimex** (Goldstern Sol)

PGE<sub>1</sub> (50µg) 0.05 ml  
+ Papaverine (75) 2.5 ml  
+ phentolamine (5) 0.5 ml  
+ Saline 1-2 ml  
(4.25 ml)

dose 0.25 ml - 1 ml

**QuadrimeX**

1/2 Atropine (100 µg)  
+ 50 µg Atropine (270 µg)  
+ 2 Atropine (20 µg)  
+ 4 Atropine (4 µg)

Atropine (10 µg) (10 µg)

dose: 0.1 - 1 ml

• Better to be  
avoided for  
Fear of  
Severe Cardiac  
Complications

NB  
The Best used single Agent is:  
PGE while the best of all (single  
or combination) is **Trimex** or  
Goldstern Sol.





• Other less commonly used drugs: لا شائعة  
فعالية

- CGRP
- VIP
- Na - Nitroprusside

Dose & preparations: [1] when using Single Agent:

• Papaverine: 30-120 mg (usually 30-60 mg)

• Phentelamine: 0.5-1 mg

• PGE: 10-20 mg

[2] Using Combinations:

**Bimex**

تولين

Rigith + Papaverine (1:30)  
(1 mg) + (30 mg)

↓  
prapism

NB phentelamine +  
replaced by  
chlorpromazine.

**Trimex**

(best  
mix)

PGE<sub>1</sub> (500) 0.05 ml  
+ Papaverine (75) 2.5 ml  
+ phentelamine (5) 0.5 ml  
+ Saline 1.2 ml  
(4.25 ml)

dose 0.25 ml - 1 ml

**QuadrimeX**

1/2 atropine (100 mg)  
+ 1/2 atropine (270 mg)  
+ 1/2 atropine (20 mg)  
+ 1/2 atropine (4 mg)

↓  
Atropine (4 mg)

dose: 0.1 - 1 ml

↓  
• Better to be  
avoided for  
Fear of  
Severe Cardiac  
Collapse

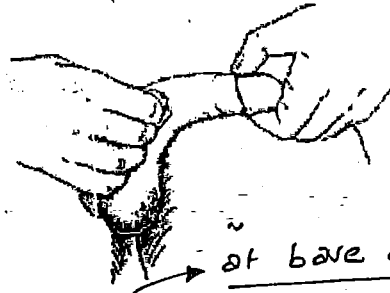
NB  
The Best used single Agent is:  
PGE while the best of all (single  
or combination) is Trimex or  
Goldstein Sol.

# TECHNIQUE OF ICI

either  
Bt

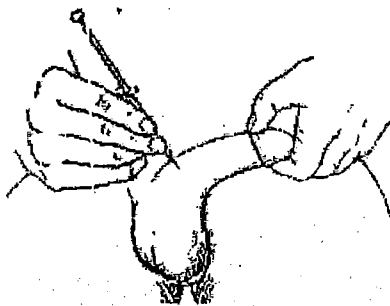
Androgen: <sup>مركب هورموني</sup>  
استر  
insulin Syringe

- ① Use injection site as illustrated. This area is designated on the drawing with the crosshatch marks. & rubber band is put at base of penis to ↓ escape of drug to circulation.



at base of penis

- ② Locate the area of injection. Wipe off with an alcohol swab. Grasp the head of the penis, not the skin. Position the penis along your inner thigh. Maintain traction on the head after cleaning the side of the penis



- ③ Grasp the syringe between the thumb and middle finger like a pen. Place the needle on the site of injection at a 90 degree angle. Push the needle in, gently but firmly, all the way down to the hub.

تقريباً  
90 درجة

## ④ Site of Inj.

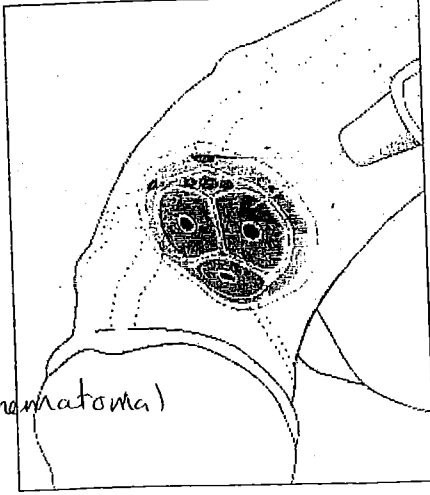
at dorsal aspect of base at 2 & 10 o'clock

avoid inj. at   
 12 o'clock → Urethra injury  
 3 → at septum (hematoma)  
 Penile aa & Ns injury

during inject: 2 resistance sites are felt: at skin & Tunica.

if persistent resistant → indicate that the needle cross the opposite side of Tunica (Septum).

Penile Injection Technique



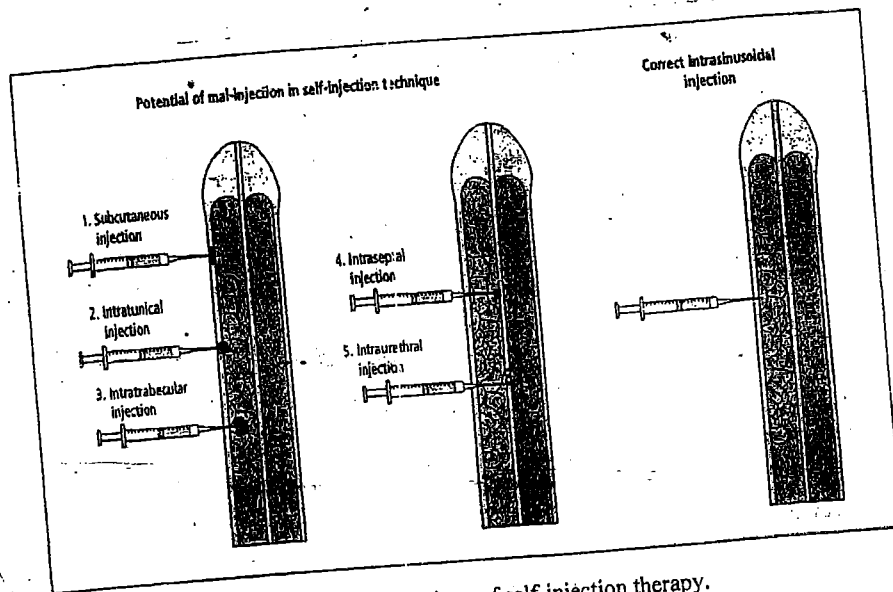
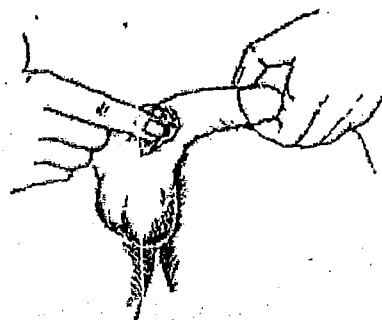


Fig. 18.4: Technique of self-injection therapy.



Remove the needle. Apply pressure with your index finger on the injection site and your thumb on the opposite side of the penis. Apply pressure for 2 minutes. (or 7 min in coagulopathy pt).

Evaluation of response  
(w/o or of PLE)

- E<sub>0</sub> = No response
- E<sub>1</sub> = Elongate
- E<sub>2</sub> = Partial Tumescence
- E<sub>3</sub> = Full
- E<sub>4</sub> = Partial Rigidity
- E<sub>5</sub> = Full

(not full)

NB:

- ① 2 should be combined & ICI testing <  $\frac{CIS}{pelvic exercise}$  ??
- ② if used as therapeutic, Not > 3 times/w or 1/day

Interpretation of the test

→ See Arterogenic ED

## Indications of ICI

### Diagnostic For:

1. ED : to diff. bet <sup>organic</sup> & <sup>psychogenic</sup>  
 . rapid, Simple, Cost effective

2. PD : to detect the penile deviat<sup>n</sup>

3. Combined with other diagnostic tests

- . PPDU
- . Arteriography
- . Cavernosography
- . Cavernosometry.

### Therapeutic ED PE

[ very effective  
 Nearly in all Types  
 of ED ]

#### ① Psychogenic ED

relieve performance anxiety & restore Spont. Erect<sup>n</sup>

#### ② Organic ED

(program of preCital self inj.) ± followed by Spont Erect<sup>n</sup> ??

- . ↓ performance anxiety
- . Good tissue oxygenat<sup>n</sup>

#### ③ used in # of PE

(see PE).  
 premature ejaculat<sup>n</sup>

## Contraindications

- ✓ Hypok<sup>as</sup>emia
  - ✓ Coagulopathy
  - ✓ Glaucoma

- ✓ Intolerance to Hypotension
- ✓ Severe psychiatric illness
- ✓ Poor vision or Manual dexterit<sup>y</sup>
- ✓ Morbid obesity → difficult to inject
- ✓ Anticoagulant # (relative C.I.)
- ✓ Glaucoma & BP (Papaverine)
- ✓ Severe ← systemic dis  
Blood dis  
Venogenic ED  
PD.

# Complications of ICI

Priapism

Isch-  
-emic

Non-  
Ischemic

How??

Veno-  
occlusive

injury

Myelitis

Pain (PGE1)

Priapism  
Pain (PGE1)

• Trauma  
• Systemic  
• Psychogenic

① Prolonged Erection & Priapism

② Pain:

Common = PGE1 (add Procain)  
mild & don't interfere w/ course  
only 3? discontinue d.t. this pain

③ Fibrosis:

most serious & late complication  
incl. PGE1 (1%) [why? -- TGFβ --> Fibrosis]  
papav (12%) [why?? d.t. acidity of  
papaverine w/ ppt  
at alkalinity of blood.]  
proper technique ↓ it

if occur

stop HI for 2m for possible spont. improvem.  
then repeat inj.  
again under proper clinical & conographic follow up.

if no spont. improvem.  
& or there is Tachyphylaxis

stop ICI & shift to another line.

④ Faulty inject

→ trauma  
injury of Urethra  
Nervous bundle  
sinusoidal walls  
corpus segum → hematoma  
late fibrosis

⑤ Systemic complications

✓ Hypertension (d.t. systemic abs) more e-  
✓ Hepatotoxicity (" " " of papaverine)  
✓ Tachycardia

⑥ Psychogenic Complications: lack of satisfact d.t.

✓ (1) Anxiety about injects pain & complications  
✓ (2) " " " artificial Nature of Erects

Suitable doses

PGE1 (1%) (Papaverine) (1%)  
Bimex 1 (7%)  
use PGE

# VCD (Vacuum Constriction Devices)

Indicate organic ED & Refusion of implant or ICI

structure:

Vacuum Chamber  
(Cylinder)

جهاز سيزم في القفص  
على شكل قفص  
القفص

3 basic elements

Negative pressure  
Pump

Connected to the Cylinder

→ -ve pressure →  
Pushing of Blood to  
Fill cavernous tissue  
(erection like state;  
NOT true erect  
as there is no dilatation of Cav.  
Tissue.)

Tension Rubber  
band

Moved along the  
Cylinder to base

3 pens to  
Entrap Blood into  
it (then)

Chamber remains  
& coils started

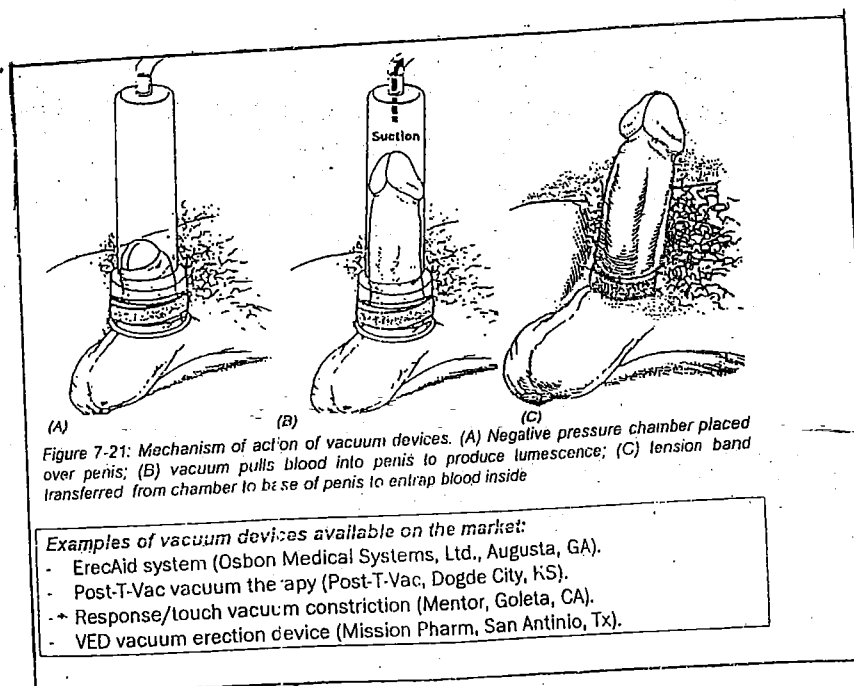
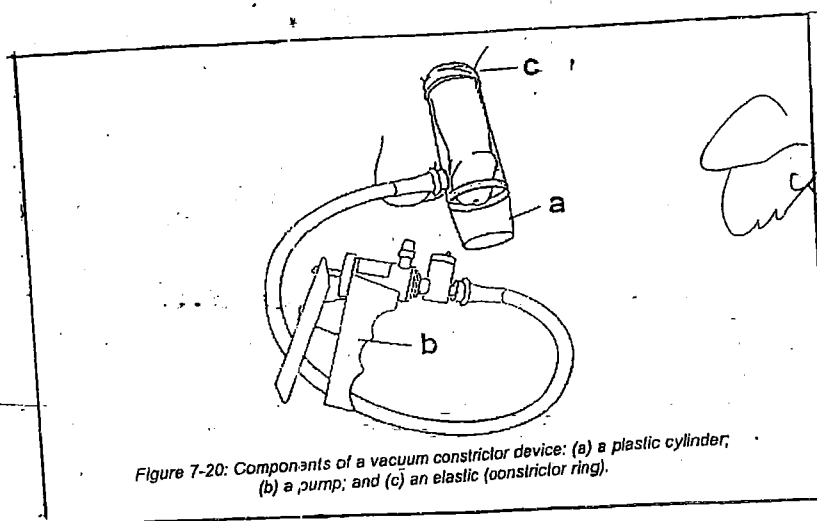
[band not  
only to base  
> 30 min. → isch.]

Complication:

- ① Pain & Erythema
- ② Pulling of scrotal skin into Vacuum cylinder (if large sized)
- ③ Cohesion & Blood dis. & Coagulation
- ④ -- 3 Ejaculate (by ring on base of penis)

Advantage: minimal invasion & complication. So + preferred  
by many patients.

Disadvantage: (1) lack of spont. Erect  
(2) dissatisfaction



## Penile prosthesis (Implant)

121  
(Ref. Penile  
implant for  
ED 2007 by  
Narindra).

### Indications:

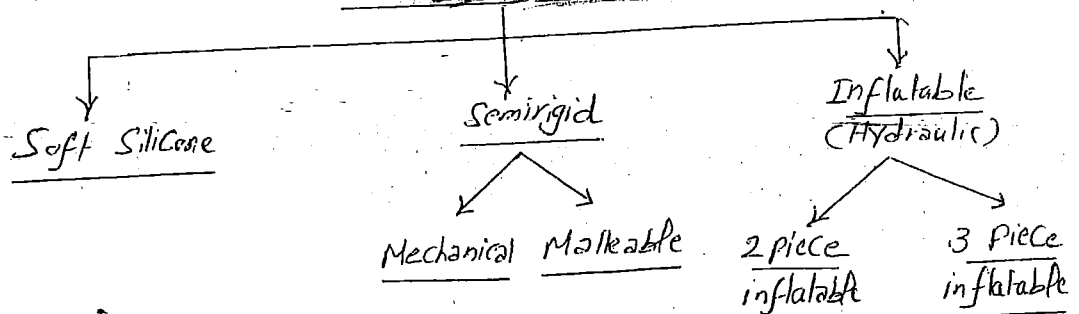
Any Patient with ED &/or deviation (that prevent intercourse) after failure &/or unacceptance of other less invasive measures as:

- . Oral Therapy
- . ICI
- . VCD

so indications  $\pm$

- . DM
- . RF
- . Neurogenic ED
- . Vasculogenic ED
- . Peyronie's dis
- . priapism
- . Psychogenic ED (after failure of sex therapy & other Measures).  
     deep psychosis  $\rightarrow$

### Types of penile Implants





122

## 1- Soft Silicone Implant

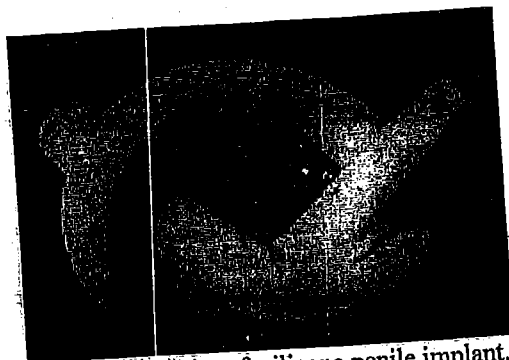


Figure 6. Virilis soft silicone penile implant.

→ inserted in c-c.  
→ indicated in spongy  
erectile tissue

- \* Currently these devices are manufactured in France and sold under the names "SSDA" and "Virilis" in a number of countries.
- \* This implant is indicated in the presence of residual spongy erectile tissue which permits tumescence and complementary girth expansion around a central silicone support.

## 2- Simirigid

A- Mechanical:



Figure 5. Dura II mechanical penile implant

articulating segmen  
held by central  
ring covered by  
silicone  
jacket

- \* Structure: articulating segments of polyethylene held together by a central spring and is now sold by American Medical Systems. (Figure 5) These articulating segments are covered by a polytetrafluoroethylene sleeve surrounded by a silicone outer jacket to prevent ingrowth of tissue into the prosthesis parts.
- Advantage: 1- better concealment (during day time activity).
- 2- no spring back after bending

Disadvantage: excessive bending may lead to damage. rupture

123

A- Malleable (rigid enough for coitus and malleable for daytime concealment):

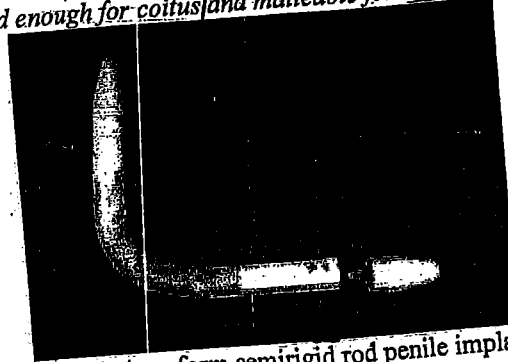
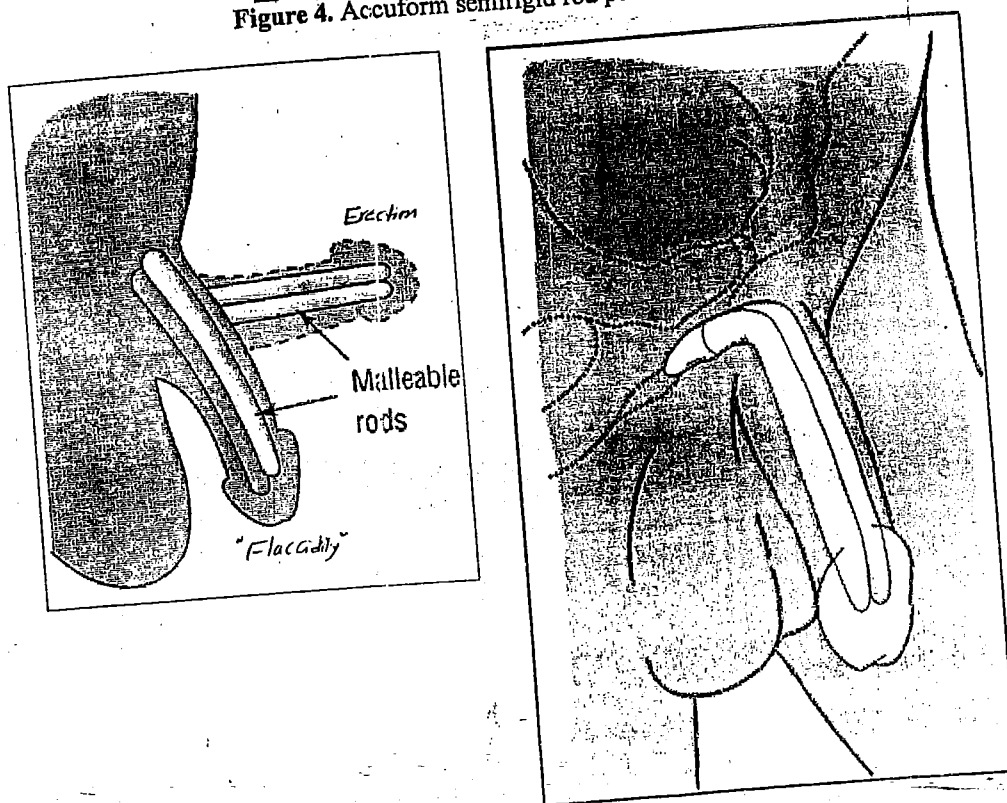


Figure 4. Accuform semirigid rod penile implant.



- \*Structure: braided silver wire surrounded by a silicone coat.
- \*Advantage: 1- cheap, easy implanted  
2- less incidence of mechanical damage <sup>No</sup> (less than inflatable)  
3- suitable for Peyronie.
- \*Disadvantage: 1- Penile flaccidity, concealment, and girth are not optimal.  
2- More liable to erosions in neurogenic ED. (arg)

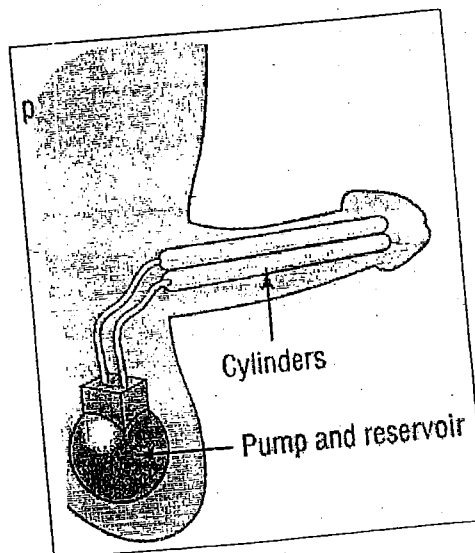
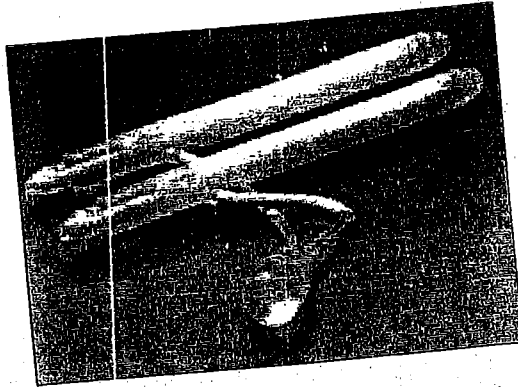
The rods are usually placed through circumcision-like or penile-scrotal incisions.

### 3- Inflatable:

The inflatable implant is a common penile prosthesis that's more physiological.  
The inflatable devices are either:

- **A One piece inflatable prosthesis (Dynaflex model):**  
 \* Double roads device composed of 3 parts: proximal reservoir cavity, central mid chamber and distal pump at glans.  
 \* when erection desired press the pump at glans → fluid transfer from the reservoir to the central mid chamber → inflation  
 \* Deflation done by steady bending for 10 seconds → fluid will pass from the chamber to the reservoir.

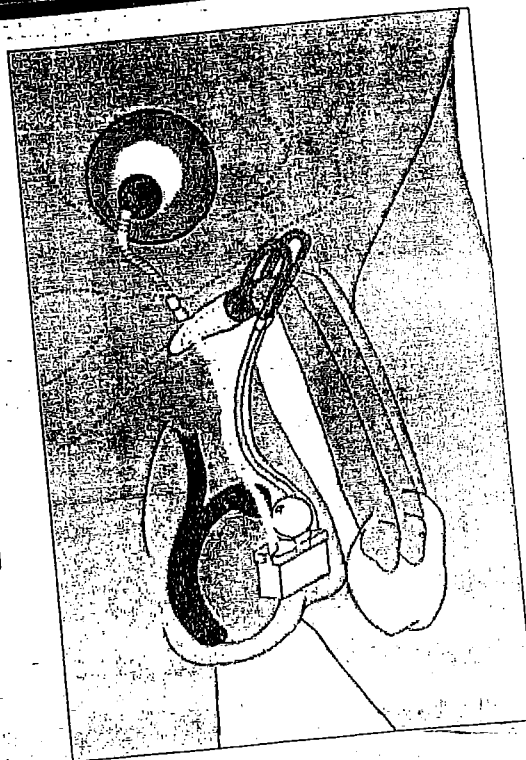
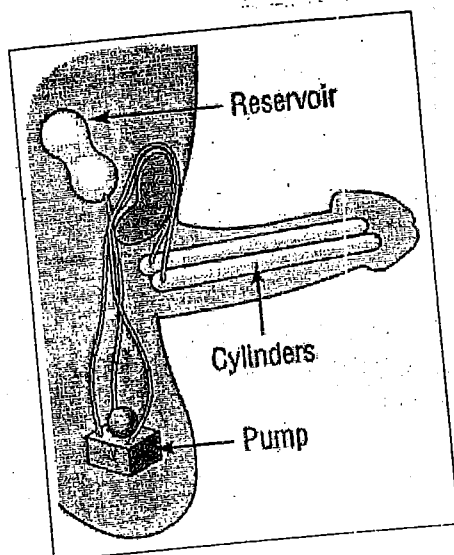
- **B Two piece inflatable prosthesis, the pump and reservoir are in the scrotum and**  
 are used to inflate the cylinders into the erect position. The cylinders are then deflated by pressing a valve at the base of the pump to return the fluid to the reservoir



⑥ **Three piece inflatable prosthesis**, the pump is in the scrotum and the reservoir is in the abdomen.



125  
 - pump → scrotum  
 - Reservoir → abd  
 → chamber cylinders → penis shaft



\* Implantation of the multicomponent inflatable prosthesis requires placement of inflatable cylinders into each corpus, the reservoir into the perivesical or preperitoneal space, and the pump into the scrotum (on the right side for right-handed patients, on the left for the left-handed).

\* This device connects through a tube to a flexible fluid reservoir and a pump. The pump is shaped like a testicle and inserted in the scrotum. When the pump is squeezed, the fluid is forced into the inflatable cylinders

20

implanted inside the penis, producing an erection.

\* Both types increase in girth, and the three-piece devices also increase in length.

\* The inflatable cylinders produce a more natural effect. The patient is able to simulate an erection by using a pump located in the scrotum.

\* Two-piece systems are particularly useful for patients in whom placement of an abdominal reservoir would be difficult or impossible. They are also somewhat easier to place surgically, but produce approximately 80% to 85% of the girth change and rigidity of the three-piece unit and less flaccidity when deflated.

disadv. : damage.

## • Basic Surgical Technique (procedure)

A. Strict Aseptic Conditions: <sup>أسترجع</sup> to prevent the most important & serious complication (inf.): ?

- ✓ (1.) H of any septic focus eg SKM or UTI.
- (2.) Shaving ! pubic area. "علاوة على"
- (3.) Antibiotics:

قبل العملية، أثناء العملية، وبعدها  
 Vancomycin + Gentamycin

or: Cephalosporines + Quinolones.

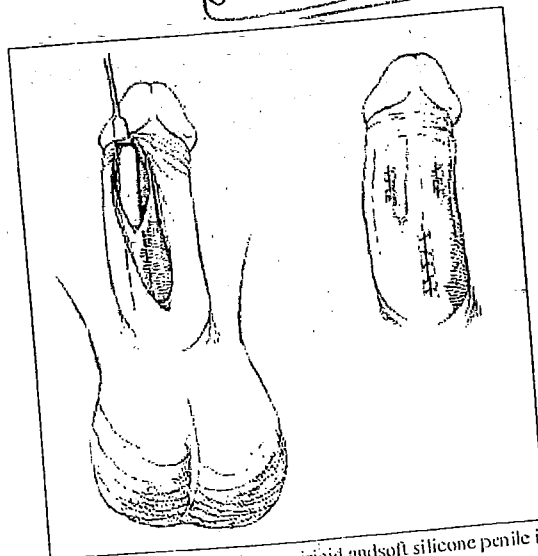
(4.) Continuous wound irrigation during operation.

B. SKM incision: <sup>في ثلاث طرق</sup>

- (1.) Dorsal Sub Coronal
- (2.) Infra Pubic.
- (3.) Ventral (Perioscrotal) (الرجل):

• less incid of (inf) & (scarring)

good healing



Ventral penile: approach to placing semirigid and soft silicone penile implants.

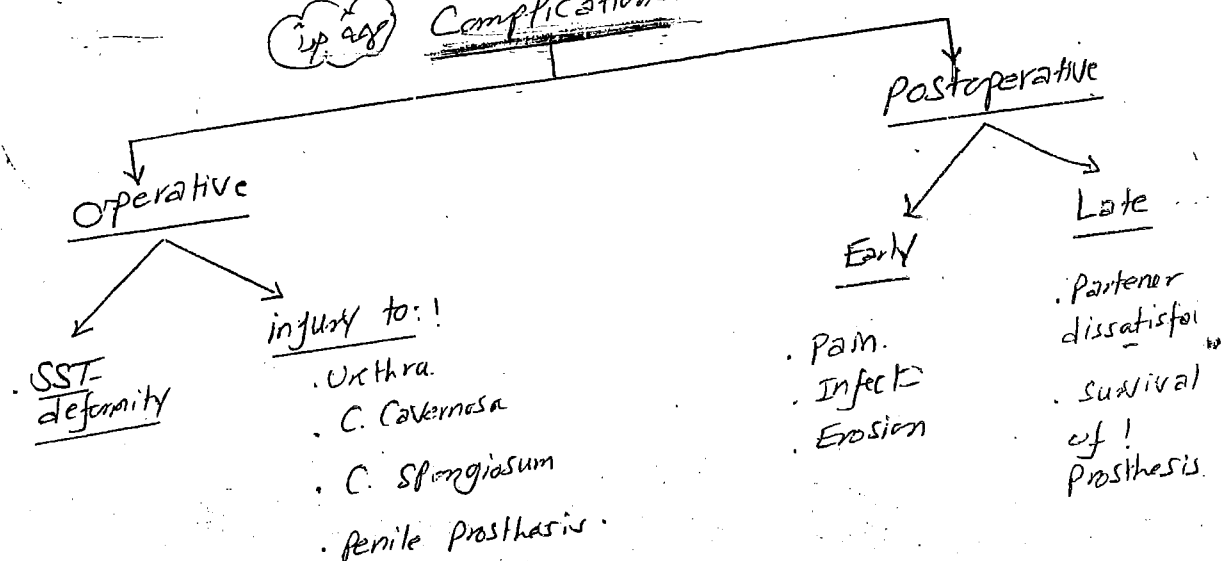
### C Corporal incision & dilatation

incise each Corpora longitudinally.

Hegar dilator is introduced (#7 - #13)

### D Insertion of prosthesis: suitable sized rods are inserted. Followed by closure.

### Complications



### A Operative Complications:

use of jet air

#### 1. SST Deformity (Supersonic Transport aircraft):

inadequate dilatation of Corpora dilatator too short rods insertion → flaccidity of glans over! distal

end of prosthesis → Pain & difficult insertion

Downward Curved.



H: Approximation sutures bet. dorsal surface of penis & the subglandular Tunka to direct it dorsally.

129

## ② Injury to:

(i) Urethra: usually distal makes of difficult dilatation  
 postpone operation in

م: في حالة تضيق أو انسداد في الطرف البعيد من مجرى البول

(ii) C. Cavernosa: d.t. thin dilator or forced dilator against fibrotic areas.

injury ±:

- distal: → Extrusion of prosth.
- proximal: → Migration of prosthesis to perineum.
- septal: → Cross perforation.

(iii) C. Spongiosum: by surgery or Tight Dressing  
 Common in diabetics & → ischemic necrosis of penis.

(iv) Penile prosthesis: → damage.

## ③ Postoperative Complications

① Early Complications: (Pain - inf., Erosions):

(i) Pain: NLY mild perineal pain occurs in 1st 2ms but if severe or persistent > 2ms, indicating:

- Inf.
- Too long prosthesis ( )
- Diabetic neuropathy.

(ii) Infection: (Most Serious & Important Complication)

• incid.: ab - 0.98%

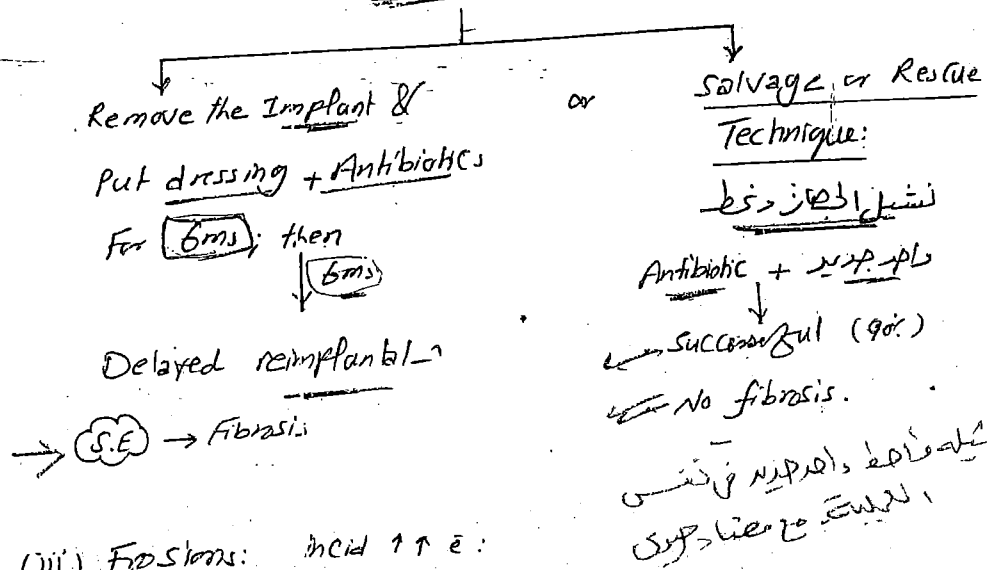
• Risk pb.: [ DM ✓  
 Immunosupp ✓ ] [ UTI ✓  
 SCI ✓ ]



organism: Staph - E. Coli or Anaerobes

- CIP: . persistent pain ✓  
 . purulent discharge ✓  
 . prosthetic Erosion ✓

II: Either prophylactic (new) or  
 Curative (revision)



- (iii) Erosions: incidence ↑ ↑ ↑  
 . ↓ Sensation (DM)  
 . Urethral stricture  
 . Radiation  
 . Cs  
 . Semirigid Type

## 2 Late Complications: Psychogenic

(i) Partner dissatisfaction: to avoid it:

. ED: ± treated w/ oral, ICI, VED.

. orgasm: ± need 1 year to develop

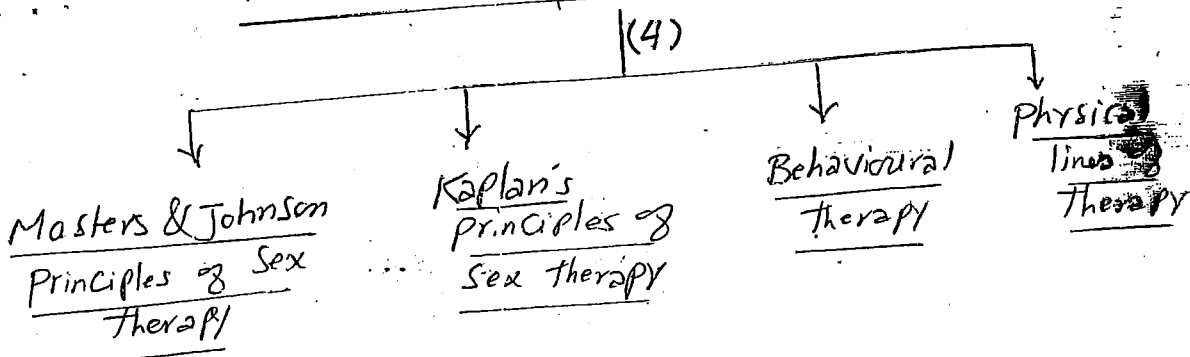
. Penile length: ✓

(ii) Survival of the Implant: 5% of inflatable Implants  
 Needed to change after 5Y

(d.f) Mechanical Complications.  
 damage

# Treatment of psychogenic ED

131.



A. Basic principles  
أبواب

B. Basic Technique

C. Specific Techniques

## Masters & Johnson principles of sex therapy

A. Basic principles  
(For all sexual dysfunctions)

أبواب عامة لجميع المشاكل

oral  
manual  
↓

1. العلاقة الجنسية لا تعني intercourse = هناك أشكال أخرى من العلاقة  
2. الجنس ليس شئ يفعله الرجل للمرأة ولكن شئ يفعله كلاهما  
3. لا يفرض الرجل

Many culture < Ideas & Attitudes are misleading

the Causes of sexual dyf. are common & are not usually related to deep psychopathology.

١٣٢  
 ٥ قد لا يتم كثير سبب Sexual dysf. طريقة وليس علاج  
 حركته لأجاء

٦ Using Past feelings & behaviour to predict  
 the underlying causes is not helpful as it may  
 limit the freedom to change

٧ There is No : such thing as uninvolved Partner  
 when Sexual dysf. exists.

٨ من سبب إلقاء اللوم على طرفين على أنه سبب في فشل العلاقة  
 الطبية

٩ Assuming Responsibility For one self  
 rather than delegating this responsibility to one  
 Partner is often effective in correct = 8 Sexual dysf.

١٠ Sex is highly intimate form of Communication &  
 relationship so it is highly related to other  
 aspects of relationship bet. Partners.

١١ developing the awareness of the feelings of the  
 other Partner will improve their relationship.

١٢ و يجب التعرف على الأشياء من أجل علاج بعض الجوانب التي قد تكون  
 على اكتساب كثير من نواحي العلاقة بينها



Aim: Allowing → Gradual Sexual Exposure  
 & to help the partners to concentrate  
 on sexual Sensations & Satisfaction more  
 than Sexual Performance → ↓ Performance  
 Anxiety & Pressure.

Method: "Sensate Focus Program"  
 (Jacobson & Anand)

Sensate Focus I

Partners are instructed to  
 stimulate each other by:

- Kissing
- Petting
- Caressing

with Complete Exclusion

of genital Areas. They are instructed  
 to concentrate mainly on Satisfaction  
 & Pleasure & Free Communications

So that each partner can guide the  
 other one about the excitatory  
 & inhibitory behaviour.

Sensate Focus

II

The same instructions  
 in the previous  
 step without  
 genital stim.  
 is allowed but  
without Intromission

# © Specific Techniques (For ED)

After Completion of Sensate Focus I & II

↓  
Intromission is

allowed if there is

good Erect<sup>n</sup> .. but if there is less

rigid Erect<sup>n</sup> the ♀ may gently ++ the penis

(to assure the ♂ that he can  
Assure his Erection many Times  
even after he lost it.)

↓ Then

Intromission in ♀ Superior Posit<sup>n</sup>

& she can guide penis in Side Vagina

to ↓ performance pressure &

anxiety helping him to stop his

"مراقب" { Spectator role about his Erect<sup>n</sup> }

↓

Stop intercourse before orgasm

& orgasm can be reached by

manual stimulatio<sup>n</sup>

↓

Intercourse in ♀ Superior Posit<sup>n</sup>

& reaching orgasm.

↓

Male Superior position

130

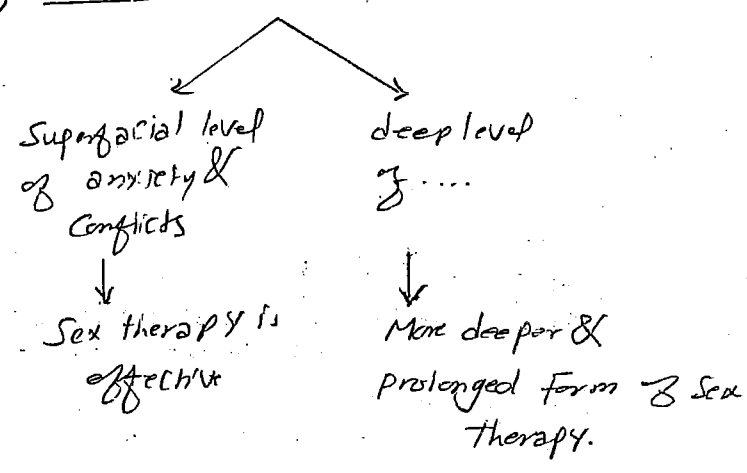
# Kaplan's principles of Sex therapy

She put similar principles of sex therapy  
 But she added:

## ①. Inhibited sexual desire Concept:

- difficult to be treated
- may be ass. to deeply seated psychopathology.

## ②. Sexual problems caused by



## Behavioural therapy

depends on principles of Master & Johnson. are few differences as concentration:

- [A] densensitization Techniques → to ↓ anxiety
- [B] Relaxation Techniques → ↓ Tension by Specific Breath & Exercises

## Physical therapies

- Viagra
  - Yohimbine
  - ICI
- Allowing him to do sexual intercourse → ↓ Anxiety & ↑ confidence

منشأ

## Ejaculation & its disorders

- physiology of Ejac.
- Disorders of Ejac.

### Q Physiology of Ejaculation

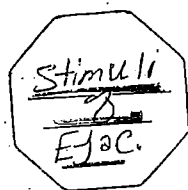
Def.

Stimuli

Neural Pathway

phases

Def. Neurophysiological reflex occurring simultaneously with orgasmic feeling.



#### Central (Cerebral)

Stimuli

There are Cerebral Centers for Ejac.

Ejaculation may be:

stimulated by:

stimulation of Cerebral Centers

Sexual Fantasies  
imagination

Inhibited by

• Fears  
• Psychic Trauma.

#### Peripheral (Genital)

Stimuli

Rhythmic tactile stim.

of  $\left\{ \begin{array}{l} \text{glans} \\ \text{shaft} \end{array} \right\} \rightarrow \text{ejac.}$

& this can be stimulated or inhibited by the aforementioned Cerebral Centers.



# Neural Pathways

## Sympathetic

Efferent motor impulses from  
(T10 - L2) → Hypogastric plexus →

unstriated ms. of   
 Prostate  
 S.V  
 Vas  
 BN (ejac)  
 Bladder neck

## Phases of Ejac.

## Somatic (< Sensor Motor)

Genital stim. → afferent sensory impulses along pudendal N. → S2,3,4 -  
 Efferent motor along the pudendal N. → pelvic floor & perineal ms. Ischi Bulbo

## 1st phase = Emission (Sympathetic)

def Expulsion of Seminal fluid from vas prostate into post. urethra. SV

## 2nd phase = Ejac. proper (= Antegrade ejac.) = Ejac. proper (Somatic S2,3,4)

def Expulsion of Seminal fluid from post. urethra to outside of the penis.

## Events (3 Contractions) (الانقباض)

- Contraction of   
 Int. urethral sphincter → shutting off 1 BN (so no RGE)  
 Ext. urethra sphincter → shutting off 1 prostatic urethra (so become closed space).
- Contraction of smooth ms. of prostate, Epididymis, VD → Emission of prostatic sec. & sperms (1st Fraction = Split Ejac)
- Contraction of smooth ms. of SV → SV secretion (2nd Fraction)

2nd phase :

(Ejaculation proper or Antegrade ejac.) = Ejection  
= Expulsion  
(S<sub>2</sub>, 3, 4) ✓

2 Events

Reflex relaxation  
of Ext. Urethral  
Sphincter

Rhythmic contraction of  
striated perineal & pelvic fi-  
ms. (Ischio- & bulbo-  
cavernosus)

Ejac. of Semen From  
The Penis

NB

① The ~~emission~~ phase can be voluntarily controlled &  
once Emission occurs to prost. urethra →  
Ejac. become inevitable

② Prostatic Sec. (الغدة البروستاتية) → Spermatozoa →  
SV (المني) Split Ejaculate

اضطرابات انقاج

Disorders of Ejaculation

Overactivity

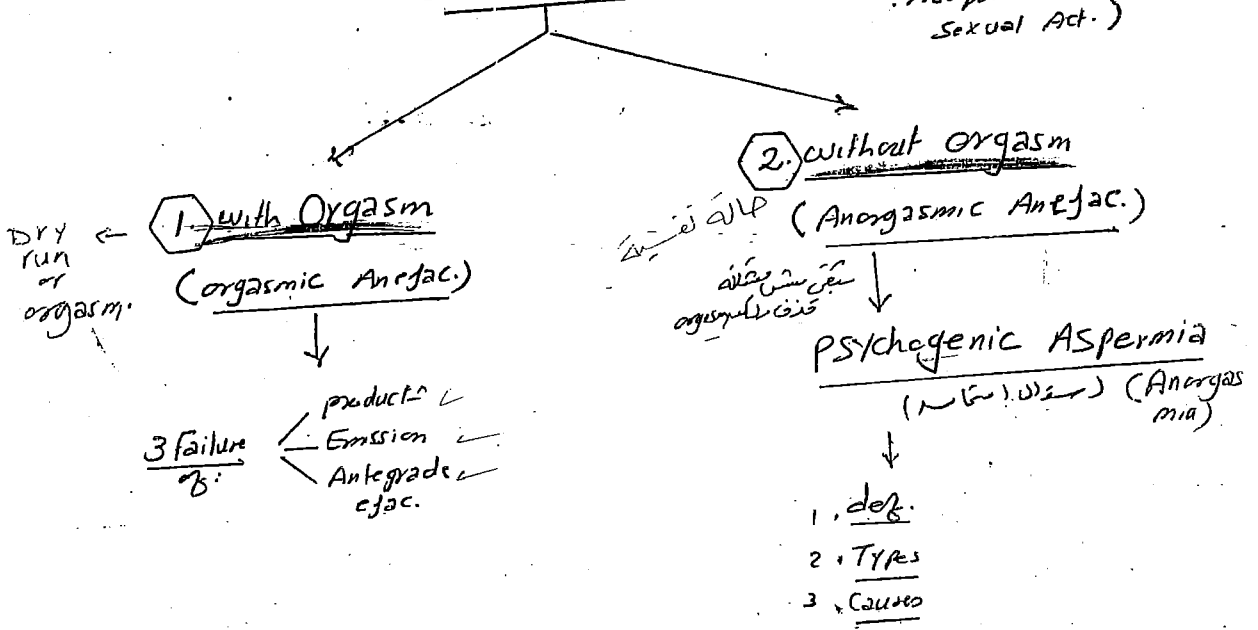
PE

deficiency

- Anejaculation
- Retrograde ejac.
- Retarded ejac.  
delayed

# Anejaculation (Failed Ejac. despite:

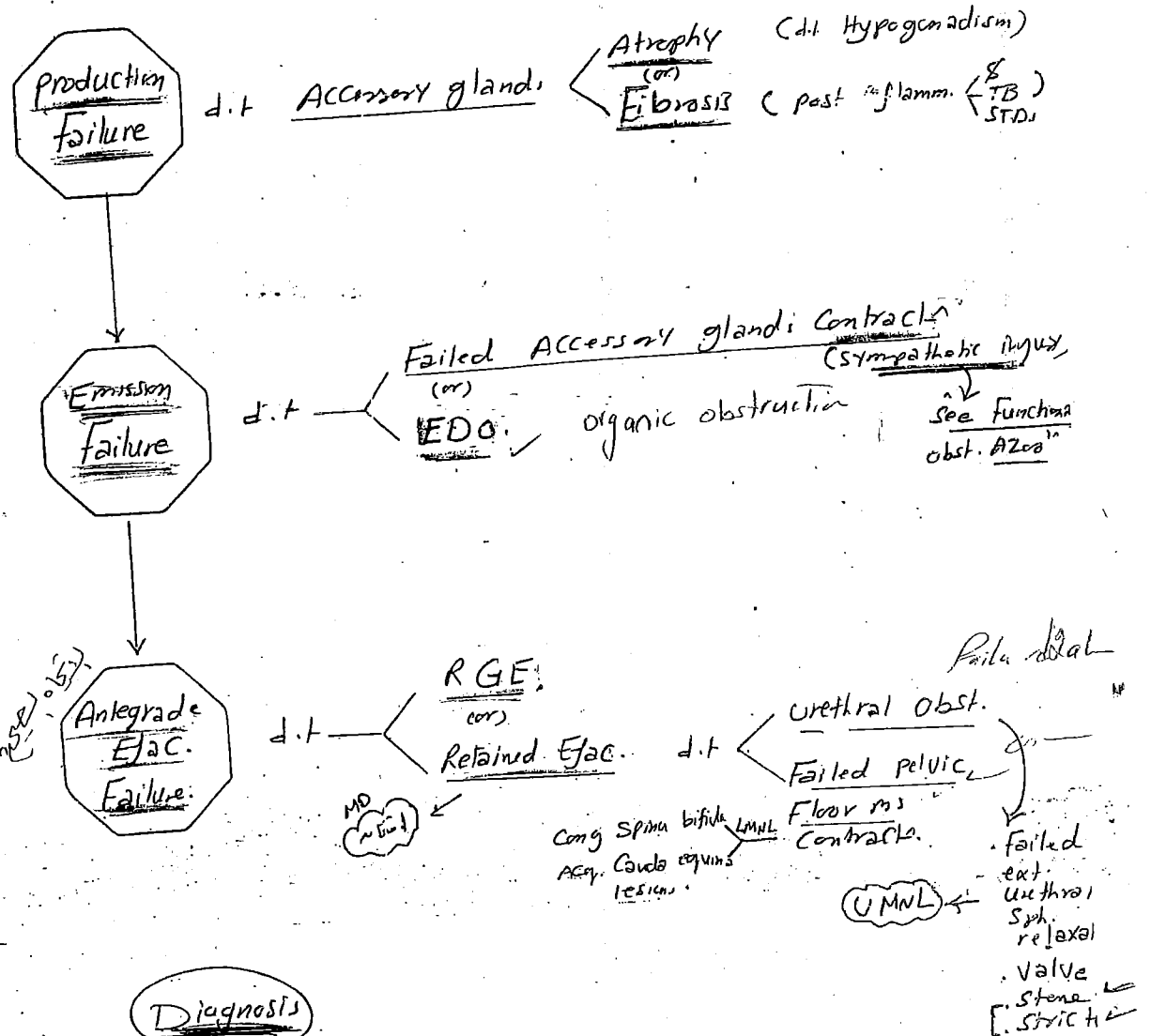
- Sufficient Erotic Stimuli
- Good Erection
- Adequate duration of Sexual Act.)



## 1. Anejaculation with Orgasm (Orgasmic Aspermia)

- AET 3 Failure 8:
  - product
  - Emission
  - Antegrade ejac. d.L.
- RGE or Retained Ejac.

• NLLY: Semen is produced  $\xrightarrow{\text{then}}$  Emitted  $\xrightarrow{\text{then}}$  Antegrade ejac.



Diagnosis

1. Hx & Exam:

Antejac. + non viscous semen + Fructose -ve &  
 -ve Postcoital urine for sperms → Failed Emission

2. Lab.

Post Coital Urine for sperms; if +ve → RGE  
 Severe oligo or AZO. → EDO

3. Rad. : For

EDO  
CBAVD → Renal Imaging

- Hx  
 (of Cause)
- ① Stop Drugs.
  - ② # of RGE.
  - ③ TURED for EDO
  - ④ Electrojac.ulator
- For Failed Emission.

See Impotence

Emission film

• EDO → TURED

• Sympathetic

(1. Drug

(2. Erector Jac.

(3. Prosthetic Massage.

(4. Sperm extract

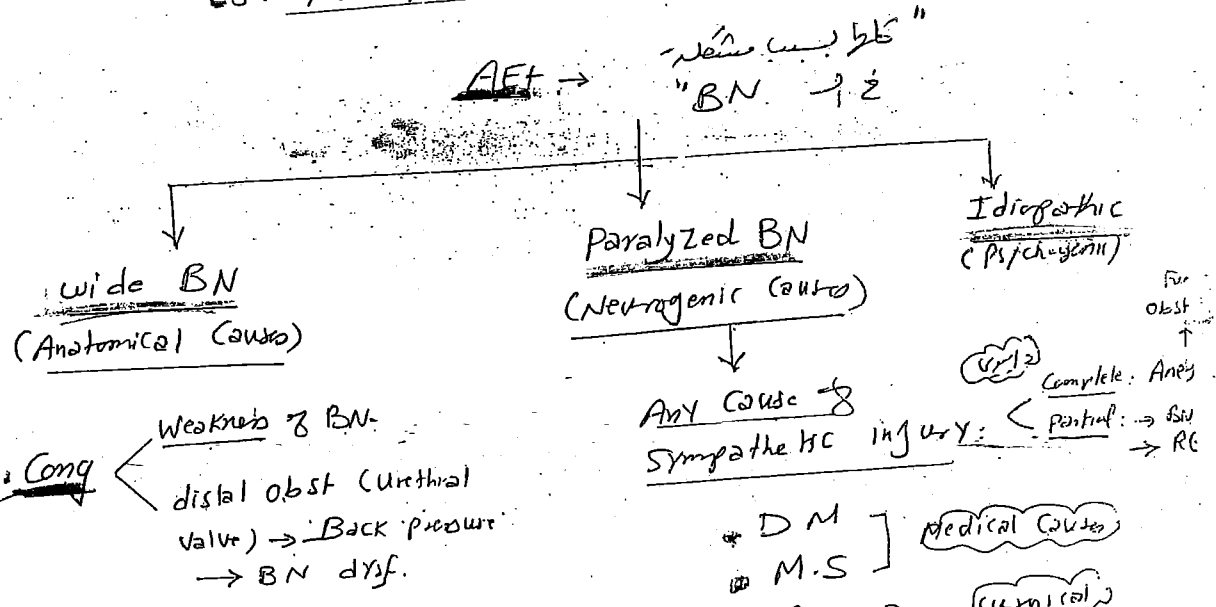
قذف العكس

# Retrograde Ejaculation (RGE)

(Cryptospermia = dry Run = dry orgasm)

def Condition in w there is Normal Emission but not in its Antegrade direction d.t retrograde Flow in UB.

- ch by
1. Commonest cause of Aspermia (Anjar.)
  2. occurs in 1% of infertile Patients.
  3. NL orgasm (injar) ✓
  4. Color of urine may be cloudy.
  5. +ve postCoital Urine for Sperm ✓  
Fructose ✓

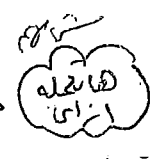


## B. Post operative:

- TURP transurethral radical prostatectomy.
- correction of BN obst. by
- Y-V plasty (Commonest)

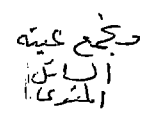
C. others Pelvic Fracture — stricture Urethra  
Meatal Stone — ext. Urethral stricture  
d.t UMN

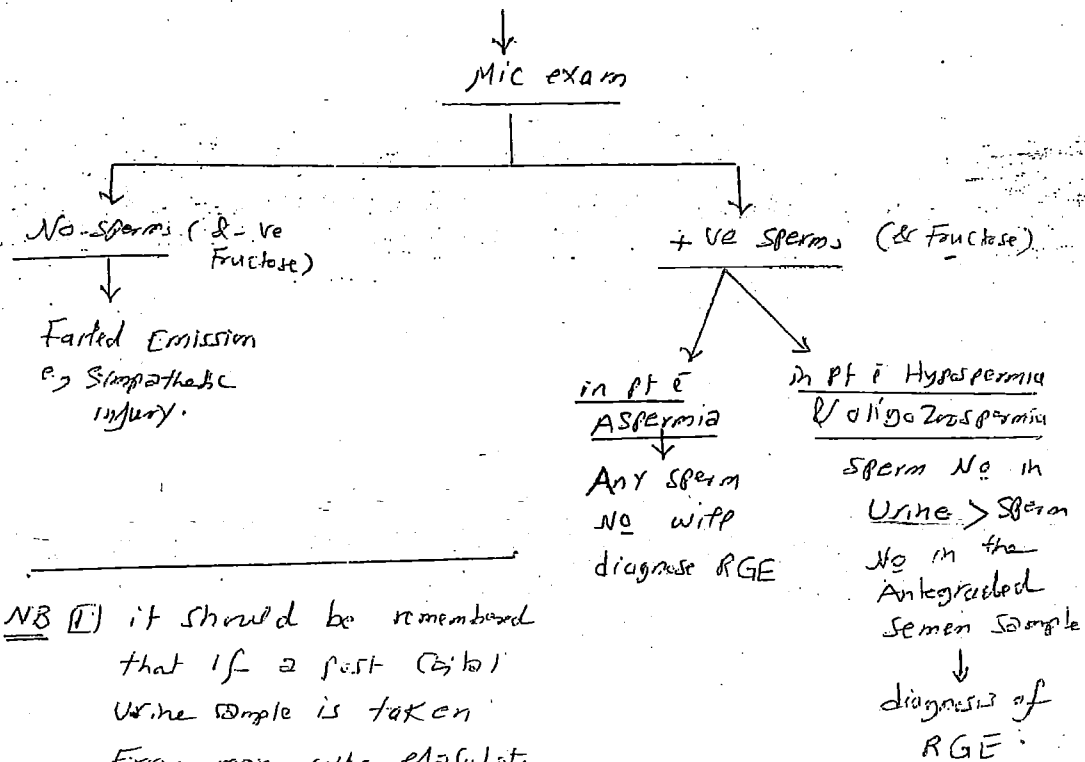
## Criteria For Ø:

- ① NL orgasm + Hypospermia or Aspermia.  
 ② +ve postejaculatory urine for  $\left\{ \begin{array}{l} \text{Sperm} \\ \text{Fructose} \end{array} \right\}$  → 

### Post-ejaculatory Urine analysis

(post coital or post Masturbate)

1. Urinate before ejaculate
2. Ejaculate (Coital or by Masturbate) → 
3. Urinate → Urine centrifuged
  - at  $\geq 300 \times g$
  - For 10 min
  - Sediment is resuspended to 1 ml.



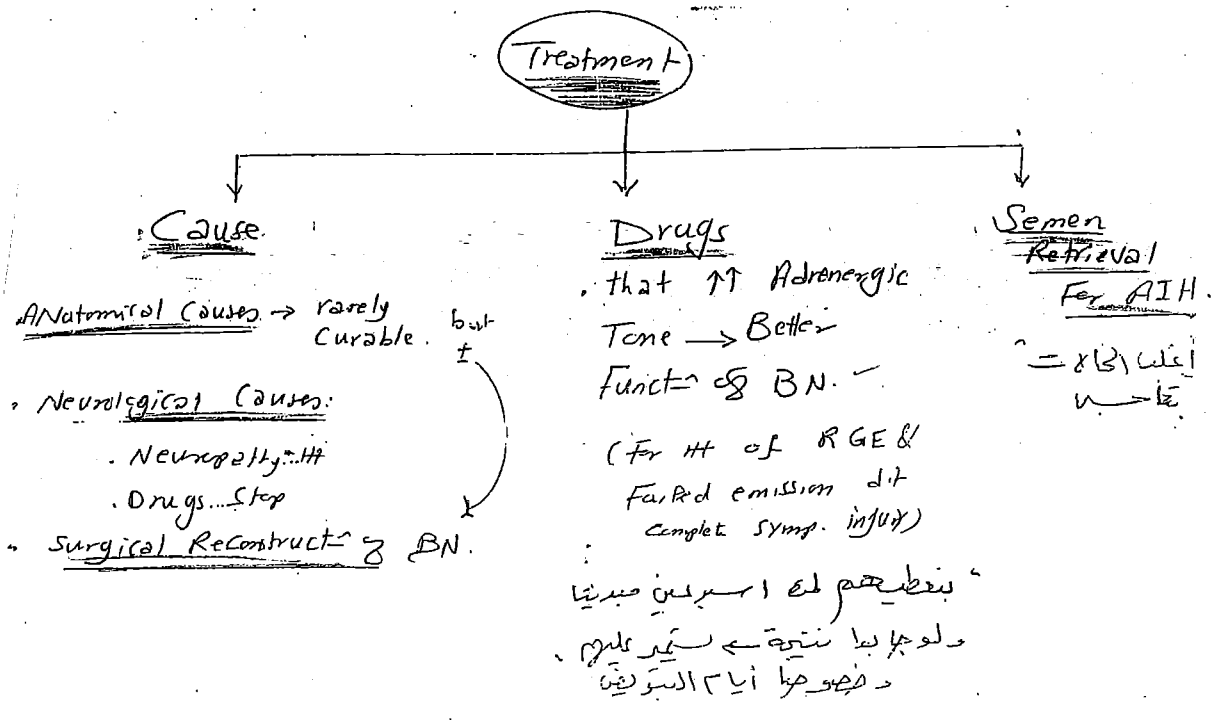
NB ① it should be remembered that if a post coital Urine sample is taken from men who ejaculate normally → +ve Urine for Sperms  
 درجه كنه  
 الكريات الحرة  
 سبق في الجري لبر

- ② Mic. exam. of post. ejac. Urine is difficult in pt i AZoos or severe oligo (so) (Fructose is preferred)

### ③ Genital Reflexes Exam (to detect Sympathetic injury):

- Inf. Hemorrhoid (L1,2) → <sup>suprapubic</sup> A. Ext. Anal Reflex: Stroking the perianal skin → Contract of Ext. anal sphincter.
- hypo-gastric pressure N. → B. Int. Anal Reflex: Introduction of Finger to anus (PR) → Contract.
- C. Cremasteric Reflex: Travel through ilioing. & genitofemoral N. (L1 & L2)
- D. BulboCavernosus (S2,3,4 = Pudendal) Squeezing the glands (dorsum) → Contract of ext. anal sphincter

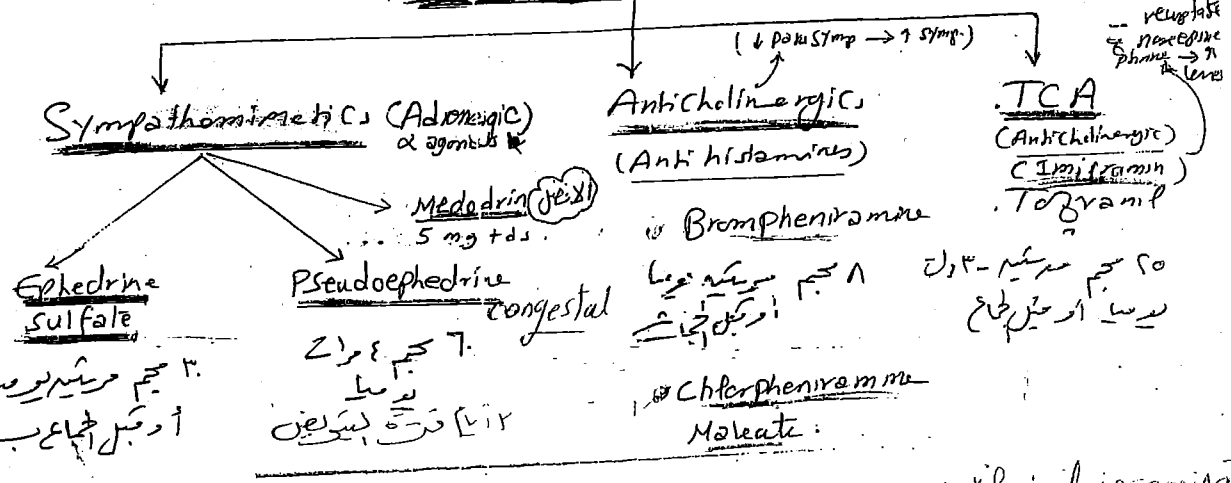
### ④ Cystoscope & Urethroscope : to detect the AET.





1. M ← (1) III of cause  
 ② Medication  
 ③ sperm retrieval

### Drugs For RGE

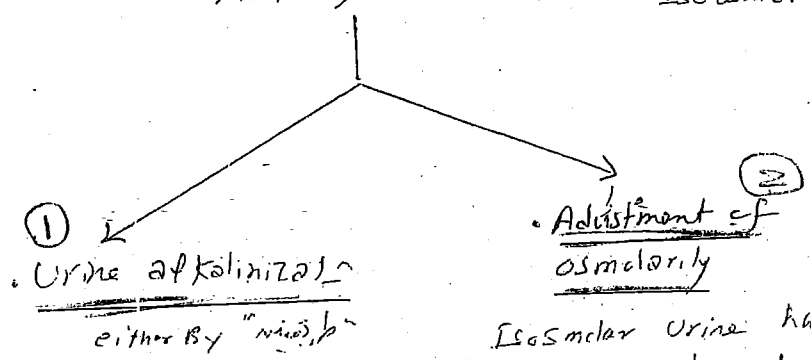


### Sperm Retrieval For AIH in cases of RGE

Artificial insemination by husband

Urine has deleterious effects on sperm motility & Morphology due to Acidity & Osmolarity

So it's essential to adjust the pH (to become 7 or Alkaline) & the osmolarity (to become Iso osmolar)



NaHCO<sub>3</sub> (sodium bicarbonate)  
 6-7 gms. 3-4 times a day  
 optimum milieu for sperms  
 Bladder irrigation by 120 ml Ringer glucose or BWN

Isosmolar urine has specific gravity ≈ 1.01  
 assessment of specific gravity of urine of pt:  
 if < 1.01 → Fluid restrict.  
 if ≥ 1.014 → ↑ fluid intake  
 So the urine become Iso osmolar

## Steps For AIH in cases of RGE

Abstract (1) (2) (3) (4) (5) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39) (40) (41) (42) (43) (44) (45) (46) (47) (48) (49) (50) (51) (52) (53) (54) (55) (56) (57) (58) (59) (60) (61) (62) (63) (64) (65) (66) (67) (68) (69) (70) (71) (72) (73) (74) (75) (76) (77) (78) (79) (80) (81) (82) (83) (84) (85) (86) (87) (88) (89) (90) (91) (92) (93) (94) (95) (96) (97) (98) (99) (100)

Adjustment of pH (Alkaline - 7.2 to 7.8)

Adjustment of osmolarity

Antibiotics

Bladder is emptied prior to ejaculation

Bladder emptied immediately after ejaculation

urination  
↓  
ejaculation  
↓  
urination

منه نقل sperm  
قد -

Semen processing

washing & concentrate

the sample (ideally < 25 ml) + 25 ml capacitating & buffering medium to Hams F-10 (to ↓ any harmful urine components)

↓  
Centrifuge for 10 min

↓  
(b) Supernatant is discarded & the sperm pellets (L5) are reconstituted in the same Hams F-10 solution using 0.5 - 2 ml

↓  
IUI or

IVF/ICSI

(if No of motile sperm < 10 million)

## Treatment of Anejaculic

### According to the Cause

(1) Failed product : d.t Hypogonadism → TRT

(2) Failed Emission

① EDO → TURED Transurethral resection of ejaculatory duct

② Sympathetic injury →

A. Drug therapy as for RGE

B. Electrical therapy,

C. Prostatic Massage

D. Surgical Sperm Retrieval

(3) Failed antegrade ejaculic

A. RGE H

B. Retained ejaculic (acc. to the cause)

### Treatment of Failed Emission:

A. Drug therapy : as in RGE.

⇒ B. Electrical therapy

Electro-vibratic

Electro-Ejaculic

# ① Electro Vibrator (Electro Vibrator) [Penile Vibratory stim. (PVS)]

Indication: SCI level at T5 or below it.

Technique: placing the vibrator at dorsum or  
Frenulum of glans penis → ++ dorsal penile  
Nerve → S2,3,4 → reflex ejaculation.

placing the probe on shaft or perineum → Not effective

Vibrator is maintained for ~ 2-3 min or  
until antegrade ejaculation occurs

↓  
if failed wait for  
1-2 minutes & repeat

↓  
if failed

↓  
auxiliary Method: +

✓ use of 2 vibrators

✓ Abd. Electrical stimulation added

✓ oral Sildenafil before PVS.

## Advantage

علاج طبيعي  
لا يتطلب دواء  
IOT 2

## Disadv. → Autonomic dysreflexia:

• Patients with injury at level of T6 or above

→ uninhibited sympathetic reflex

→ HTN      Sweating

• Bradycardia      chills

• Headache.

• Stroke, Seizures or death.

• Prevention is HT or Nifedipine.   
 (السعال الجاف)

C.I: untreated HTN or Cardiac dis.

(2) Electro Ejaculator (EEJ)

if PVS failed → EEJ (95% success of semen retrieval)

General Anesth (Lat. decubitus)   
 ويتم إدخال الجهاز (probe) من طرف آخر ← ينشغل بجهاز نبضات كهربائية

Max  
5-25 wlt  
& 10-20  
stimulats)

⊕ — angrade ejac or RGE → so Alkalinization of Urine is done before its use (as in RGE).

to detect any rectal mucosal injury. ← Proctoscope   
 لازم بفحصه وسيله Proctoscope

يتم تكرار العملية كل ٢ بالتبديل مع فترة تبريد للزوجة

The Semen For IUI / IVF.

[C] Prostatic Massage:

dist proximity of prostate to SV & ampulla; prostatic Massage may → seminal secret

chance of ejac. & obtaining Motile Sperm

[D] Surgical Sperm Retrieval: BY

- TESE or TESA
- ESA (PESA or MESA)

② Psychogenic Aspermia  
 (Anorgasmic Anejac.) = ♂ Anorgasmia (Law)

Def Disorder of orgasmic phase of Male Sexual Response Cycle ch by: recurrent or persistent ← delay, difficulty or Absent  
 of attaining orgasm following sufficient sexual stim.  
 or various personal distress.

Types ① Primary: Never achieved orgasm neither by Coitus nor by Masturbation.

② Secondary:  
 either { was NL for certain period then become Anorgasmic  
 or Selective: Anejac. occurs w/ his Partner (wife) & Not w/ Masturbation or other Partner.

③ occasional:  
 ————— { Sex { Sex

## Causes <sup>أسباب</sup>

### 1st Type

① Rigid & religious family background & prohibition of sex.

② Obsessive Compulsive disorders. <sup>اضطرابات</sup>

③ Biological Cause: There is strong likelihood of biologic variability in threshold of Arousal before Experiencing orgasm.

### 2nd Type

Ⓐ "AutoSexual Orientation"

تجسس لذته لذته  
نفسه لا يستحق  
مع العلاقة الجنسية  
مع أن...

d.t. role of  
Fantasy  
Frequency  
Motivations

So with Masturbation

there may be striking in:

Speed  
Pressure  
duration  
Intensity } Needed for orgasm

↓  
W are Not present in NL Partner  
Rebt

دوره لذته لذته

### e. Male Conditioning:

أعود على حبس لذتي أثناء الاستحمام بالصابون  
على إيقاع ملأه أثناء الجماع من قوة إيقاع ربي ما أستر  
على "Psy. Aspermia" ←

Ⓑ Others: • Fear of impregnation (✓)  
• lack of ♀ physical Attraction.

### Occasional:

d.t.:

① Lack of Sexual interest in particular Sexual Act (oral sex)

② Alcohol.

③ SSRIs.

④ Aging.

⑤ Short interval bet ejaculation

## NB Delayed (Retarded) Ejaculation

def Inability to ejaculate or to reach orgasm in a reasonable time despite NL sexual desire & sexual stimulation.

- NL men ejaculate: 2-4 min<sup>(10)</sup> from onset of Active Thrusting - during intercourse
- in delayed ejaculation: ejaculation (orgasm) may occur after  $\geq 30-45$  mins.

Incid. 1-4% of men

NB → Some consider it as a slight form of Anorgasmia (Psychogenic)

- Anjac. انعدام انقباض
- or
- Anorgasmia (without Ejac.)

سبب



Fatigue  
Alcohol

### Criteria for diagnosis of anorgasmia

1. Absence of orgasm and ejaculation.
2. Presence of nocturnal emissions.
3. Prolonged sexual act.
4. Post-ejaculatory urine shows absence of sperm.



## TM of Psychogenic Aspermia (or Delayed Ejac.)

① \* Sex therapy (2ry Type) ④

بیتعداد انه مركز على متاع طبع مسترنة  
حياة الزوجية وبتقريبها بمرور  
الزمن جازية

③ gradual sexual Exposure: & Combined manual & vaginal stimulat

ببعل استمرارية في طبع الزوجين  
شدة وجودها / لم يطع العقب في  
Vagina قبل وقتها بفترة  
منه الزوجين تالاه

Combined manual &  
Vaginal stim.

(Holding back of  
Penis while it  
inside the Vagina.)

② ElectroVibrator to obtain semen For AIH

③ Pharmacotherapy: drugs used to Reverse SSRI's  
Induced Anorgasmia or delayed orgasm:

① Cyproheptadine (Trianin)

② Vigra

③ Amantadine (200mg) [Antiviral that ↑  
Dopamine]

(Buspiron) → ④ Buspar (Anxiolytic): 5HTA1 agonist  
in pte Generalized Anxiety (15-60 mg/d)

⑤ Bupropion: ↑ Dopamine level.

⑥ Apomorphine & Yohimbine.

# NBO Anorgasmia

لر سوان امان  
هائيد مرده

without Ejac.

with Ejaculation

Psychogenic  
Aspermia.  
(کينه)

1) orgasmic Anhedonia: انعدم  
انگيز

• Sacral & cephalic lesions (Tm)  
→ Intergo efferent  
to Cortex.

Psychic:  
الام با باليك نتيجة علة  
مستنه ضيق نفس  
الام با باليك روى (فقد)

- 2) Elechoejaculation
- 3) Epilepsy
- 4) Certain spinal Tm.
- 5) Heroin & Morphine  
withdrawal.

Table 7-4: Differential diagnosis of aspermia.

| Criterion   | Psychogenic<br>aspermia  | Organic aspermia                 |   |  |  |
|---|--|----------------------------------|---|--|--|
|   |  | Production<br>failure            | Failure of<br>erission                              | Retrograde<br>ejaculation                              | Retained<br>ejaculation                              |
| Orgasm  | -  | +                                | +   | +  | +  |
| Nocturnal<br>Emission                                       | +  | -                                | -   | -  | -  |
| Duration of<br>intercourse                                  | Prolonged  | Normal                           | Normal  | Normal   | Normal   |
| Emission  | +  | -                                | -   | +  | +  |
| Postejacula-tory<br>urine findings<br>(sperm &<br>fructose) | -  | -                                | -   | +  | +  |
| Pathogenesis  | Psychogenic  | Absent semen<br>production       | Absent<br>contraction of<br>accessory sex<br>organs | Patent<br>bladder neck                                 | Anterior urethral<br>abnormality                     |
| Etiology  | - Sexual<br>ignorance<br>- Sexual<br>inhibitions<br>- Other<br>factors | Severe<br>androgen<br>deficiency | Complete<br>sympathetic<br>injury                   | - Anatomical<br>- Incomplete<br>sympathetic<br>injury. | - Obstruction.<br>- Loss of<br>contractile<br>power. |

## IV Premature Ejaculation (PE) (Rapid Ejaculation)

UP  
GHTEM

According to (DSM-IV-TR); it has 3 Criteria:

- 1 Persistent or Repeated Ejaculation  
Slight stimulation < Before, on, or shortly after penetration (IELT)

& before the person wishes it.

- 2 Marked distress or interpersonal difficulty.

- 3 Not Exclusively due to direct effects of drug or chemicals e.g. withdrawal from opioids.

### Other definitions:

Persistent or recurrent inability of the male to control the ejaculation to satisfy his female partner in sexual coital episodes provided that she is orgasmic.

MP  
Sol  
NL & orgasm

because most of ejaculate rapidly during certain period of their life.

### PE has 3 hallmarks:

- A. occurrence of ejac. prior to wishes of both partners (short IELT)
- B. Lack of sexual satisfaction
- C. Lack of self efficacy regarding the condition (inability to delay ejaculation sufficient to enjoy love making)

IELT (time elapsed bet. vaginal intromission & ejaculation); if < 1-2 mins → PE  
Intravaginal Ejaculatory latency CNL (2-4 mins)

NB the 1st definition (DSM-IV) & the 3 hall-marks:

هذه التعريفات: تجنباً عند فترة معينة للعلاقة الجنسية وللوصول  
إلى "Climax" والذي يعبر عنه استوعب به الإنسان خاصه ويعبر عنه  
عنا من عذبة خاصة بعدى إنزاله (الفرغ من العلاقة الجنسية  
على سبيل المثال:

If  $\begin{cases} \text{♂ Climax at 8 min} \\ \text{♀ (avg) Climax at 5 min} \end{cases}$

Not PE

لأنه كل من الطرفين  
حيث أنها إرضاء من العلاقة  
على الرغم من قصر العلاقة

لأنه لا ينفي . If  $\begin{cases} \text{♂ Climax at 20 min} \\ \text{♀ u at 30 min} \end{cases}$

It's PE

لأنه رغم أنه طويل فترة العلاقة  
ولكنه لم يكتش استماع بزوجته

ولذلك لا حظ أن

تعريف PE قد يترك: قدرة الرجل على إرضاء زوجته

① Control of Ejac. occurrence & satisf.

②

Delayed orgasm or Anorgasmia

the problem is in the ♀ & Not in ♂ (PE)

③ IELT has been used to measure PE in many studies. However Ejac. Control shown to mediate Patient or Partner Satisfaction & Sexual intercourse & Ejaculation-related distress.

④ IELT on those don't fit DSM overlap & IELT on those fit DSM.

NB → DSM-IV-TR

Diagnostic & Statistical Manual of Mental disorders 4th edition Text revision -- by American Psychiatric Association (2000)

## Classification of PE

### 1. Acc. to the onset:

- (a) 1ry PE → didn't experience NL ejac. before;  
 (ب) always having PE.  
 (b) 2ry PE → Acquired PE after a NL period  
 of good ejaculatory control.

### 2. Acc. to the Frequency:

- (a) Selective → with specific partner or sexual act  
 (ب) occasional → occurring once in a while (د.ت)  
 Fatigue or mental stress.  
 (c) persistent or recurrent → in > 50% of intercourse.

### 3. Acc. to the Type:

True: real loss of ejaculatory control

False: The ejac. is NL in Time but

There is  $\rightarrow$  orgasmic dysf. or  
 Sexual Ignorance.

♀ Female Anorgasmia

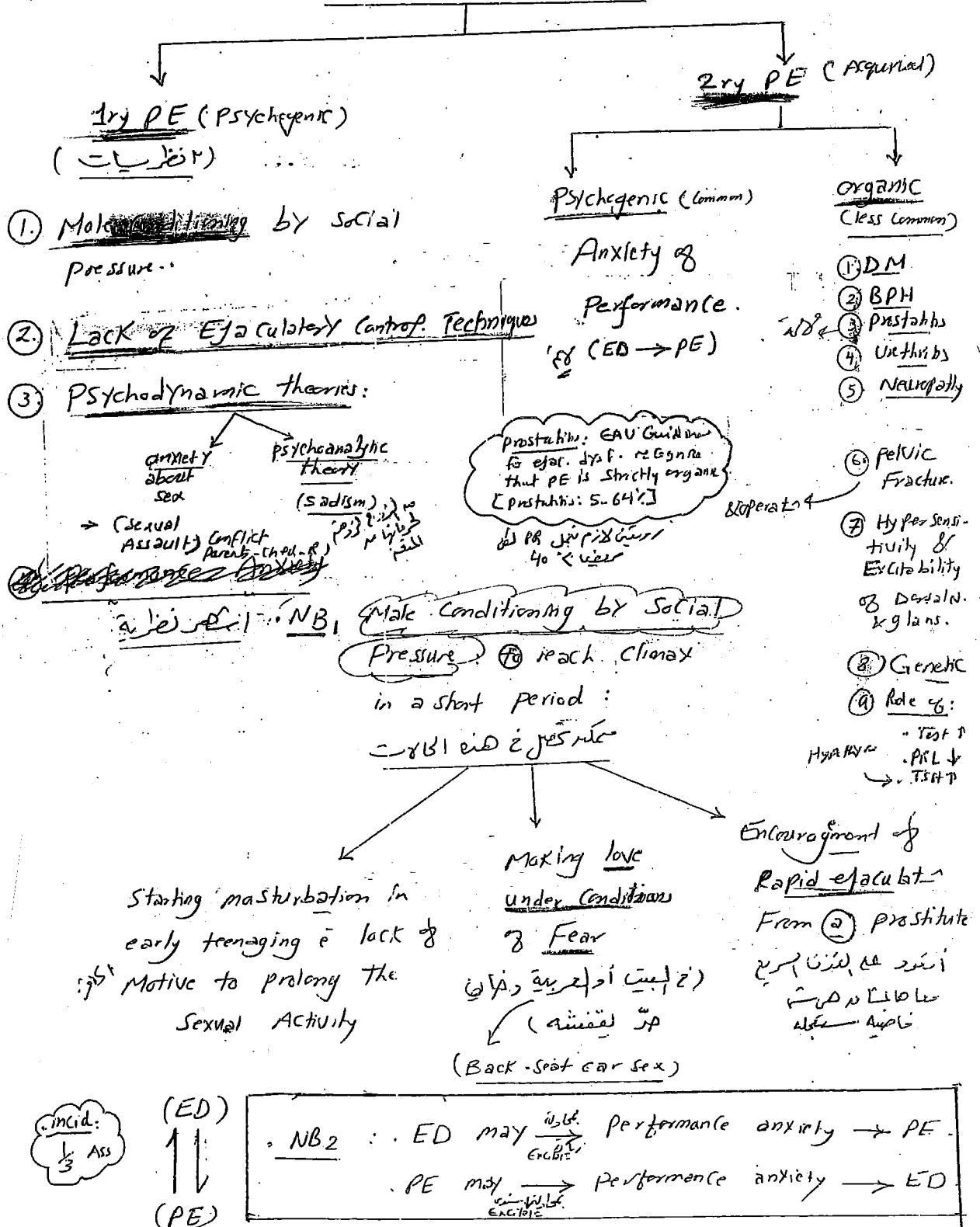
### 4. Severity

Mild: IELT 30 - 60 seconds

Mod: " 15 - 30 seconds of vaginal penet.

Severe: after before sexual activity or in < 15 sec.

## Causes of PE (Most cases are psychogenic)



## NB (B) lack of ejaculatory control techniques: (Controversial)

تکنیک‌های مهارت در کنترل انزال (موضوع بحث است)  
 ۱. thought distract (تفكير را منحرف کردن)  
 ۲. pelvic floor m. contract (عضله کف لگن را منقبض کردن)  
 ۳. alterate depth & speed of vaginal thrusting (تغییر عمق و سرعت دخول واژینال)

## (C) psychodynamic theories: (نظریه‌های روان‌پوی)

### 1. Anxiety about sex d.t:

- Family incest (زنا محاربه)
- Sexual assault
- Conflict w one or both parents (تعارض با یکی یا هر دو والد)

### 2. unresolved & Excessive narcissism:

during infancy → exaggerated importance being placed on penis & associated pleasure of urination.

### 3. Psychoanalytic theory: deep sadistic wishes of some men towards the women that make the men punish her by depriving her from pleasure or by scolding her.

## (D) Performance Anxiety: (Fear of failure to satisfy the ♀)

(A) ED: if the ♂ is afraid that his Erects will not last. d.t < previous ED or Imagined Failure pot of → PE. the patient may have used the phrase "Honey, you Excited me so much I just couldn't hold back"

بسیار زیاد من را هیجان زد که نتوانستم نگه دارم

(B) ♀ may belittled him with comments as "You must not be much of a man since you can't stay hard until I'm satisfied" → performance anxiety & → PE. [in addition she may have difficulty in achieving orgasm through intercourse & may require clitoral stim. (لوسش فوجت ده) → always Failure of Her Clital Satisf.]

اینکه من را اینقدر  
 شاد نگه نمی‌داری  
 پس مرد خوبی نیستی

## Complications of P.E

- ① in males → 2ry ED
- ② in females → Orgasmic dysf.  $\Rightarrow$  impaired Sexual interest
- ③ Deterioration of sexual or marital relations

PE يهيئ المريض على تآكل في العلاقة الزوجية ← فبعضها ليس  
 من العلاقة الجنسية ويقتضيها فبعضها الزوجية أنها لم تفرق  
 جنسياً من حيث (شياء) لظواهرها الزوجية، فنقدنا للعلاقة الزوجية

## DD ① Female Anorgasmia:

average time for ♀ Climax is  $\approx$  12-25 min  
 So in anorgasmia or severe delayed orgasm  
 of ♀ → nearly all men have PE.

- ② Drug induced PE: resolved by Drug stop.
- ③ Prosemen or pre Gme

## للأكثر فئة (HL) Biochemical Factors in PE:

من خلال دراسات أقيمت:

- ① High T. level  $< \frac{\text{Total}}{\text{Free}}$  seen in PE pt.  $> NL$
- ②  $\uparrow \downarrow$  level of PAP &  $\alpha$ -glucosidase in PE pt  $> NL$   
 (So Epidid. & Prostate dysf. may → PE).

- ③ Hypoprolactinemia: may → PE  
 ED  
 Anxiety  
 Metabolic Synd.

Men's lowest  
 quartile  
 level of PRL.





# Mechanism of Action:

→ **A** In PE antidepressant TCA  
SSRIs

**TCA** → unknown mechanism but ± d.t.

Serotonin →  
inhibits sexual  
function

① -- autonomic process involved in  
ejac. & Erection (Antiadrenergic & cholinergic)

② ↓ Psychological Arousal

③ Anxiolytic effect

④ -- Reuptake of Serotonin → ↑ level  
Dopamine → ↑ level

Very little effect on reuptake of Norep. & Dop.  
**SSRIs** → selectively -- Serotonine reuptake  
→ ↑ Serotonin level → -- SD &  
↓ Erect → -- Ejac.

**B** Analgesics: TCA (see PHN)  
**C** Antiinflammatory & Immunomodulators:

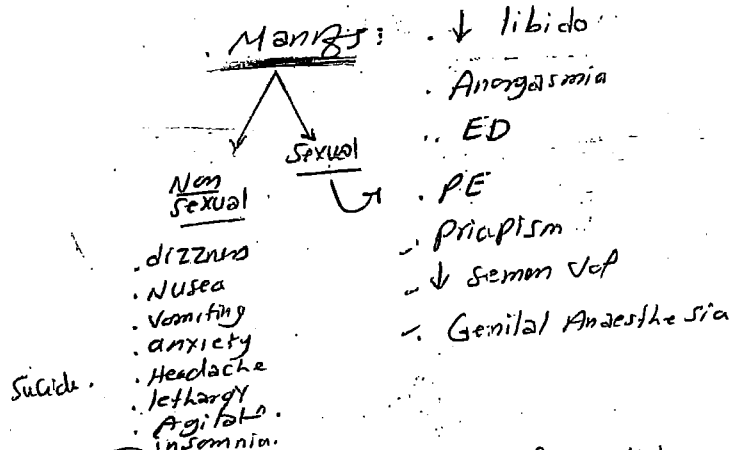
down regulate IL-6  
TNFα  
IFNγ

Sexual non sexual  
**S.E** ① **TCA**:  
(Anticholinergic manifs)  
(ALL to EL)  
drowsiness  
dizziness  
dry mouth, yawning  
Blurred Vision  
Tremors  
Rash  
Sexual problems  
Wt gain or loss.

② **SSRIs** (sexual side)  
Nausea  
diarrhea  
Agitation (early)  
Headache  
Sexual:  
↓ libido  
Anorgasmia  
ED  
Serotonin Synd  
Tachyphylaxis  
↓ 10-15

NB Serotonine Synd = Post SSRI's Sexual dysfunction = SSRI's discontinuation synd.

Sexual known.  
def: Sexual disorders occurring following discontinuation of SSRI's. That may last for mths - yrs.

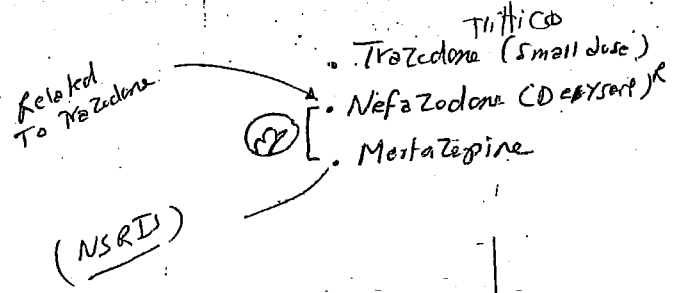


Fluoxetine → SD

Common Paroxetine  
 either d.t.  
 ↓ dose or  
 stop.

NB Sexual Function & Antidepressants:

(SSRI's) → Commonest group affecting the sexual function (↓ SD, Anorgasmia, ED)



Bupropion (Bupar)  
 Bupropion (wellbutrin)

(typical) → delay in onset of action (↓ SD & ED)

(sexual desire)  
 Drug That ↓ SD & causing ED + TCA  
 & SSRI's →  
 { . Apomorphine  
 . Yohimbine

- Doses
- Imipramine (Tofranil) → 25 - 50 mg/d.
  - Clomipramine (Anafranil) → 25 - 50 mg/d.
  - Sertraline (Lustral) → 25 - 100 mg/d.
  - Paroxetine (Seroxat) → 20 - 40 mg/d.
  - Fluoxetine (Prozac) → 20 - 40 mg/d.
  - Citalopram (Cipram) → 20 mg/d.
  - Dapoxetine (الحدث) (الأقوى) (30-60 mg/d) → 20 - 40 mg/d.
- كل هذه الأنواع يمكن استخدامها إما على طريقة

قبل الجماع

طريقة

٢. حجم الدواء صغير  
٤. لا يوجد

١. On demand → قبل الجماع
٢. Continuous → لفترة ٦ أسابيع
- المرضى في نهاية فترة ال on demand.

٢. لا يوجد  
٤. لا يوجد

يعني يمكن البدء باستخدامه قبل العلاقة الجنسية (on demand)

أو يمكن البدء بتجربة مستمرة (Continuous)

Dapoxetine  
is the  
only FDA  
approved  
drug for  
PE (Phase  
III)

Don't Forget To treat ED as well. # may  
improve PE How? If PE is 2ry to ED.

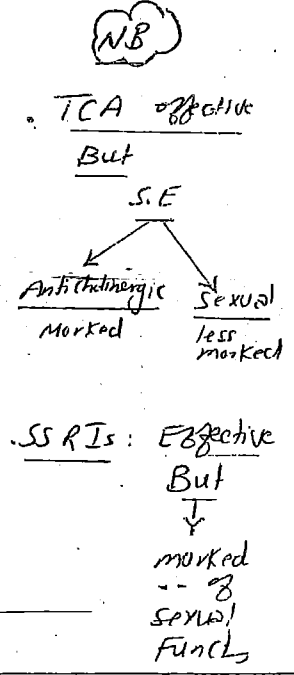
- ترتيب الأنواع على حسب القوة :
- الأقوى
- Joy Box → Paroxetine
- Clomipramine
  - Sertraline
  - Fluoxetine
  - Citalopram

كل الأنواع لا بد من سحبها تدريجياً على مدار ٤ أسابيع

علاشان تجنب  
(withdrawal  
symptoms.)

Fluoxetine

So ←  
Combine it  
with Aphrodisiacs.



## \* Viagra & PE

Can Treat PE Throug 2 Mech.

(HL)

Indirect → ① Improving ED → Improving anxiety of perform.  
→ improve PE

Direct → ②

• ↑ NO & ↓ Symp. tone

• Relaxation of ms of Vas, Epid. & SV

→ Antagonize Symp.

• ↓ Erection threshold

• downregulation of receptors involved in somatosensory latency time.

Sympathetic effect  
(sm related) ↓ Erection threshold.

Viagra + SSRIs → More S.E.

## \* Topical Therapy (local Anesthetics)

• lidocaine 2.5%

• prilocaine 2.5%

• Korean SS Cream (Herbal)

what are disadv. ??

↓ pleasure in <♀ (dt anasth.)  
ED.

[4]

\* Sex Therapy →

Sex Therapy

[5] Others

ICI → Help conventional PE

لا يوجد أدوية أخرى  
تساعد في علاج PE

Condom → ↓ penile sensitivity → ↓ PE.

Masturbation → لا يوجد أدوية أخرى تساعد في علاج PE  
تساعد في علاج PE

## → B Tramadol

Mech. 1. Centrally acting opoid analgesic

2. -- Reuptake of  $\begin{matrix} NE \\ Serotonin \\ GABA \end{matrix}$

Dose 50 mg po 12 hrs before intercourse

don't exceed 400 mg in 6 hr &

400 mg 12 hr.

Efficacy : effective

S.E : Addictive (So Not used or limited use in PE).

## → C Viagra in PE : May improve PE either by

↓

Indirectly

by improving  
ED → relief of  
performance anxiety  
→ improved PE.

Directly ??

1. Sympatholytic effect

2. down regulation of  
Rs involved in  
somatosensory  
latency time.

↓ sensitivity of  
nerves

## → D $\alpha$ -blockers ( $\alpha_1$ -) : Trazosin 5mg, 1d → 50% efficacy.

• Topical therapy  
(local anesthetics)

e.g. lidocaine 2.5%, procaine 2.5% & Korean SS Cream  
(Herbal)

disadv.  $\begin{matrix} \leftarrow CD \\ \downarrow \text{pleasure in } \begin{matrix} \sigma \\ \rho \end{matrix} \end{matrix}$

[4] Sex therapy د/ محمد عبد الله (م. ١٤٣٥ هـ)

[5] Other lines

• ICT →

يساعد على الاحتفاظ بالانقباض بعد  
القفز جنسياً على سمدرة ثانية  
والتأكد من دخول البع

• Condom → ↓ penile sensitivity

• Masturbate → يعمل على التخلص من  
الاحتياج الجنسي قبل الجماع

one or 2 hrs before sexual intercourse

(HL) علاج مع دايونين (م. ١٤٣٥ هـ)

→ antidepressant & out ED

Bupropion - Trifluoperazine

Amentadine  
antiviral

A desire

# Asthenospermia (definition...)

AET

## Proven Causes (7)

### ① Faulty Collection:

- Long Abstinence period
- Spermicidal Container
- use of Saliva, soap, any Lubricant
- exposure to extremes of heat
- prolonged incubat<sup>n</sup> in seminal plasma.

"Physiological Polyastheno"

So: Repeated analysis's under Carefully Controlled Conditions should be done.

### ② Infection:

- E.G. n<sup>o</sup> ↓ Motility
- Chlamydia
- Ureaplasma can adhere to sperm → ↓ Motility

So eradicate e Doxycycline may be ass. e ↑ pregnancy rate.

### ③ Anti sperm Abs:

Abs may induce Membrane defects → affects the Intra Cellular Ca<sup>+</sup> & ATP → ↓ Motility.

So: Asthenospermia (in) pt e Genital infect<sup>n</sup> or obst. or Trauma... etc → Test for auto Abs.

Immunological infect<sup>n</sup>

## unproved (possible) Causes (5)

- ① Varicocele
- ② Epididymal dysfunct<sup>n</sup>
- ③ Deficient factors in seminal plasma necessary for Motility.  
(Nat bicarbonate & PG)
- ④ presence of inhibitory factors in sperm & seminal plasma.

### ⑤ functional defects in the axoneme:

- defective Sperm memb.
- " ATP product<sup>n</sup>
- ↓ AC activity
- ↓ Calmodulin (Major Cat Binding Ptn)
- protein Carboxy Methylase deficiency: enzyme in tail need for motility.

## Clinical tips:

presence of Symptoms suggestive UTI or genital inf → localize Culture should be done and appropriate antibiotic therapy should be given.  
empirical antibiotic if e absence of documented inf. → no effect on Motility.



structure

④ axonemal defect:

Immotile Cilia Synd (Cry Ciliary dyskinesia)

9+0 synd.

[A] Immotile Cilia Synd:

def. AR disorder; 1:30,000. (1/2) defect in 2 genes

• DNAD1 & DNAD5 } encodes proteins of dynein arms & other links of microtubules

(Cilia) → Infertility + Triad of:

Immotile Cilia + Globo Zesp.

II Stereolizing Sperm defect.

NB Immotile Cilia Synd: 50% ass. e Situs inversus → Kartagener

• Bronchiectasis  
• Chr. Sinusitis

defects in Axoneme of Microtubules

(Cilia = Sperm tail) ±:

1. lost dynein arm (s)
2. lost Central Single Microtubule (9+0 Synd)
3. lost Nexins or radial spokes.

④ NL Sperm: Count viability but 100% Immotility

HA → ICSI

[B] 9+0 Synd: synd. e structural defect of the sperm tail, there is loss of Centrif Pair of Microtubules → Immotility.

NB Necrozoospermia:

(Circled)

Vitality < 75%

Def → Spermatozoa e No Viability

usually seen in

(Viability of Sperm < 75%)

Chr. prostatitis

unilat ejaculatory duct

obst

(ass. e ↓ semen Vol.)

• Indications to do Vitality test:

if Grade D (Immotility) > 40%

Structural

Tests < NIE stain HOST

ANA e Hypogonadism

Gen Cellular

## Types of Asthenospermia:

- Isolated Astheno:
- Oligo Astheno Zoo SP:

• Most patients w/ astheno also have associated defects in sperm production Morphology

• Sperm w/ poor Movement often demonstrate Morphologic abnormalities.

• In cases of Oligo Astheno, the diagnostic work up should be identical to the work up of oligo Zoo.

*WJN*

## OAT Diagnosis of Isolated Astheno SP.

### 1 History

- Pulm. dis
- Risk factors of antisperm Abs
- Genital inf.

### 2 Clinical ex.

- Varicocele
- epid. abnormalities
- urethral disch.
- EPS & PIR

### 3 Inv.

- Repeat analysis (x faulty Glob)
- EPS Culture
- Antisperm Abs
- Genotyping

① Markedly disturbed Motility  
in the presence of otherwise almost normal sperm parameters → clinical (97% synd.)

② if Motility < 10% →  
do EIM.



### Globozoospermia (Round head syndrome)

Def. Severe form of teratozoospermia in which the sperm head appears rounded w/ absence or defect of Acrosome.

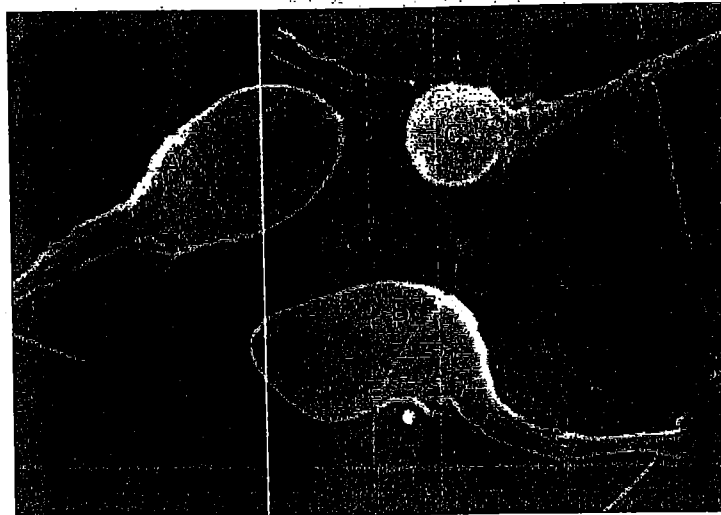
Etiology: Homozygous mutation in SPATA 16 (Spermatogenesis specific gene)

#### Types of Globozoospermia

| Complete (total) (Type I)   | Partial (Type II)  |
|---|--|
| <ul style="list-style-type: none"> <li>Complete absence of Acrosome</li> <li>No Natural Conception by ICSI</li> </ul> | <ul style="list-style-type: none"> <li>Hypoplastic Acrosome</li> <li>± Conceive Naturally</li> </ul> |

Globozoospermia + Immotile Cilia Synd → called ??

HT: ICSI (However results are poor w/ disturbed sperm-associated oocyte activation factor)



Sperm morphology is related to the fertilising capacity by in vitro fertilisation. (A=normal sperm head; B=abnormal head; C=globozoospermia—a rare syndrome in which all sperm heads lack acrosome caps and cannot fertilise)

# Cancer & Infertility

P. 93

## Mechanism of Infertility

d.t Neoplasm

Corb

### Cancer associated Conditions

#### Cryptorchidism:

2.8% assoc. F-GIS

#### Genetic: evidence of

chromosomal anomalies  
cancer pts.

### • Infertility 2ry To the Cancer itself:

#### ① Destructive effect

of Tm → severe impairment of spermatogenesis

#### ② Immunological effect:

Tm → disturbed Blood Testis barrier → Anti-sperm antibodies

#### ③ Endocrinal Effect:

in Leydig & Sertoli  
Tm → Estrogen level → infertility.

#### ④ Psychological & physical:

Stress → infertility

#### ⑤ obstructive effect: ✓

Epididymal obst.  
"by" Neoplasm.

### • Infertility 2ry to Cancer therapy:

#### ① RPLND →

Sympathetic denervation →  
[Failed emission, RGE] lack of Antegrade ejaculate

#### ② Radiation & chemotherapy:

Caused AZO → Severe oligo  
(usually 2-3 months after TH).

So Must do

Cryopreservation before therapy

• destructive  
• obstructive

• Immunological  
• Endocrinological  
• Psychological